27 August 2004

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AAAS

Science

COVER Weighing reward versus punishment. Many people voluntarily incur costs to punish unfair behavior of others. The reason for such altruistic punishment and its neural basis are discussed on page 1254. [Image: Comstock/Alamy Images]

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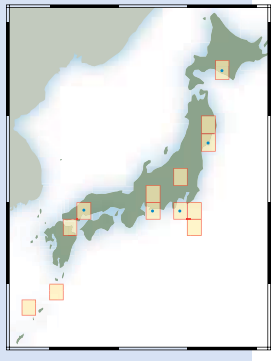

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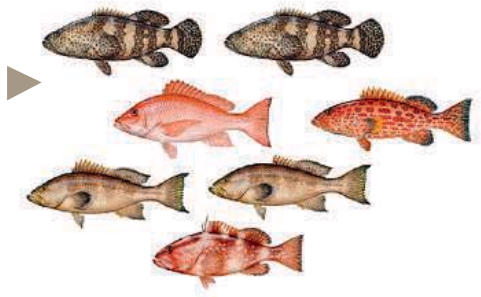

ECOLOGY: The Impact of United States Recreational Fisheries on Marine Fish Populations
F. C. Coleman, W. F. Figueira, J. S. Ueland, L. B. Crowder
Analysis of United States marine fisheries records shows that recreational fishing has been a significant, sometimes major factor in the decline of several fish stocks. *related News story page 1235*

CELL BIOLOGY: Soma–Germ Line Competition for Lipid Phosphate Uptake Regulates Germ Cell Migration and Survival
A. D. Renault, Y. J. Sigal, A. J. Morris, R. Lehmann
In developing flies, germ and somatic cells compete for the same lipid phosphate: When expressed in germ cells, germ cell migration is aided, but when expressed by somatic cells, germ cells are repelled.

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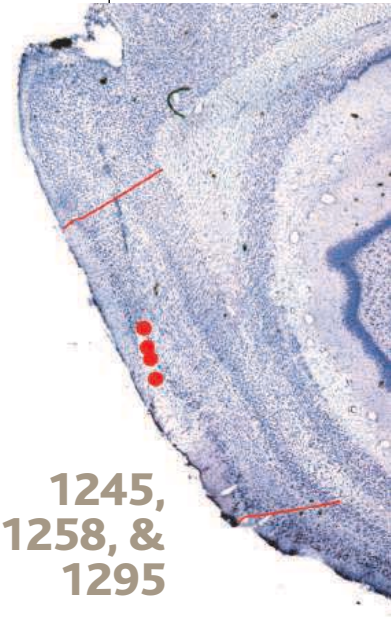

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When people punish others who are deceitful, the reward centers of the brain are engaged even if the action yields no apparent benefit. *related Perspective page 1246*

1258 **NEUROSCIENCE:** Spatial Representation in the Entorhinal Cortex
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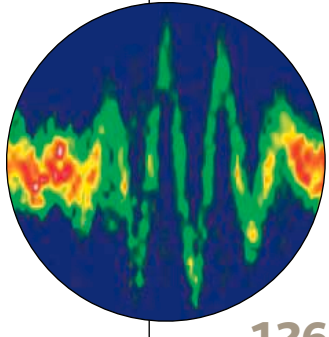

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Microlensing, in which a nearby star amplifies the light of a distant star, can reveal a stellar disk with sufficient resolution to allow direct detection of extrasolar planets.

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1277 **GEOLOGY:** Evidence for Deep Magma Injection Beneath Lake Tahoe, Nevada-California
K. D. Smith, D. von Seggern, G. Blewitt, L. Preston, J. G. Anderson, B. P. Wernicke, J. L. Davis

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1280 **CHEMISTRY:** Powering Fuel Cells with CO via Aqueous Polyoxometalates and Gold Catalysts
W. B. Kim, T. Voitl, G. J. Rodriguez-Rivera, J. A. Dumesic

Carbon monoxide, a ubiquitous by-product in hydrogen production that can poison fuel cells, can be oxidized via a gold catalyst in a fuel cell to generate electricity. *related News story page 1225*

1283 **MICROBIOLOGY:** Plasminogen Is a Critical Host Pathogenicity Factor for Group A Streptococcal Infection
H. Sun, U. Ringdahl, J. W. Homeister, W. P. Fay, N. C. Engleberg, A. Y. Yang, L. S. Rozek, X. Wang, U. Sjöbring, D. Ginsburg

"Flesh-eating" bacteria specifically infect humans because they carry an enzyme necessary for infection that binds only to human plasminogen.

1286 **MICROBIOLOGY:** E Protein Silencing by the Leukemogenic AML1-ETO Fusion Protein
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1289 **MOLECULAR BIOLOGY:** Small Interfering RNA–Induced Transcriptional Gene Silencing in Human Cells
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1292 **MEDICINE:** Impaired Degradation of Mutant α-Synuclein by Chaperone-Mediated Autophagy
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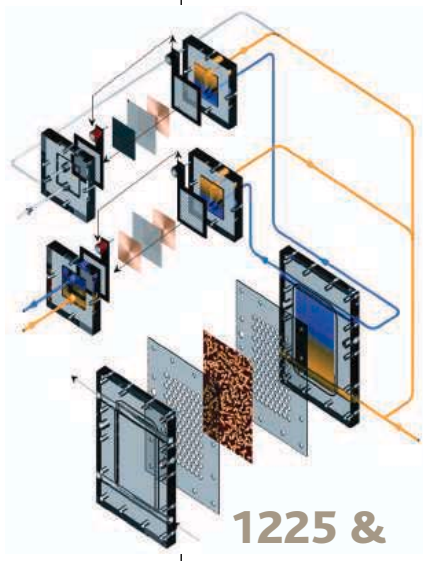
1295 **NEUROSCIENCE:** Distinct Ensemble Codes in Hippocampal Areas CA3 and CA1
S. Leutgeb, J. K. Leutgeb, A. Treves, M.-B. Moser, E. I. Moser

In rats, one section of the hippocampus codes for individual aspects of physical spaces, whereas another reacts to common features, a distinction that is reflected by different information-processing capacities. *related Perspective page 1245; Research Article page 1258*



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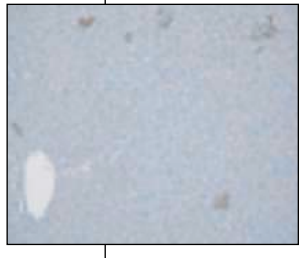

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Netherlands: Adventurous Scientists Get Room for Own Research *H. Obbink*

The Netherlands Organisation for Scientific Research awarded 88 recent graduates grants to do innovative, high-risk research.

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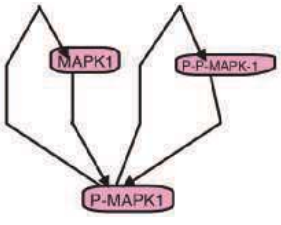

Biochemical computation of cellular networks.

science's stke www.stke.org Signal Transduction Knowledge Environment

Protocol: Quantitative Information Management for the Biochemical Computation of Cellular Networks *F. Campagne, S. Neves, C.-W. Chang, L. Skrabanek, P. T. Ram, R. Iyengar, H. Weinstein*

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THIS WEEK IN Science

edited by Stella Hurtley and Phil Szuromi

Testing a Gravity Lens

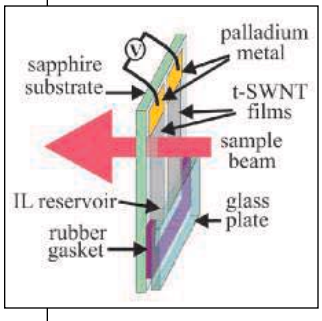
The numerous lines of sight that traverse dense stellar fields can provide opportunities for observing a foreground star aligning with a background star. Gravitational microlensing can magnify and bend the light from the background star into an annular ring image. **Abe *et al.*** (p. 1264) used the microlensing event, MOA 2003-BLG-32/OGLE 2003-BLG-219, to search for asperities in the ring image that might be created by an extrasolar planet orbiting the foreground star. They found no extrasolar planets, but they showed that the technique is precise and useful for planet searches.

Riding the Light Waves

Existing measurement techniques for characterizing light fields and pulses generally provide cycle-averaged properties, such as the frequency, wavelength, or envelope amplitude. Determining the oscillatory nature of the electric field under the carrier envelope presents a significant problem, however, not least because the electric field oscillates at around 10^{15} cycles per second for visible light. Extending the classical route of determining electric field by looking at the force on a test charge, **Goulielmakis *et al.*** (p. 1267) use a bunch of electrons created by a 250-attosecond extreme ultraviolet pulse as a probe to determine and characterize the dynamical evolution of the electric field of a several-optical-cycle femtosecond laser pulse. Having the strength and temporal variation of the electric field available should prove a useful spectroscopic tool to probe ultrafast electron dynamics within solids.

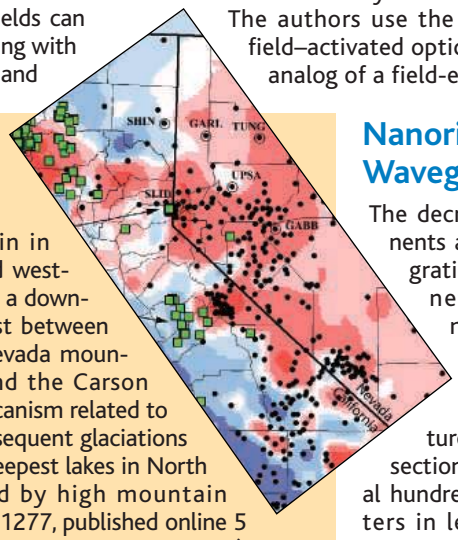
Caught on Large Films

High specific surface area, high intrinsic conductivity, and high aspect ratio are some of the outstanding characteristics of single-walled carbon nanotubes (SWNTs). These properties also enable the fabrication of highly conductive and highly transparent freestanding SWNT films. The major challenge now is making large-area films. **Wu *et al.*** (p. 1273) show they can make highly conductive, optically transparent films on the order of 80 square centimeters through a method that should be scaleable to much larger sizes. The films are prepared by vacuum filtration of a dilute SWNT solution onto a membrane. In regions where the films initially thicken, the filtration rate decreases, so there is a natural tendency to form films that are uniformly thick. The authors use the films to construct an electric field–activated optical modular, which is the optical analog of a field-effect transistor.



Deep Seismic Swarm

The Lake Tahoe Basin in eastern California and western Nevada formed as a down-dropped block of crust between the uplifted Sierra Nevada mountains to the west and the Carson Range to the east. Volcanism related to the tectonics and subsequent glaciations have left one of the deepest lakes in North America surrounded by high mountain peaks. **Smith *et al.*** (p. 1277, published online 5 August 2004) measured an extremely deep (25 to 35 kilometers) earthquake swarm beneath Lake Tahoe that was coincident with geodetic displacement measured at one station near the swarm. They infer that the two observations are related to an extremely deep magmatic intrusion, which provides information about the state of volcanic activity and the state of stress beneath the lake.



Nanoribbon Optical Waveguides

The decrease in size of optical components as well as efforts aimed at integrating them into optical chips and networks will require efficient methods for getting the light from one component to another. **Law *et al.*** (p. 1269) show that nanoribbon oxide structures, which have rectangular cross sections typically on the scale of several hundred nanometers and are millimeters in length, can be used as optical waveguides and coupled to nanoscale optical components. The strength and flexibility of the nanoribbons also allow them to be physically manipulated for the creation of complex optical networks.

Fuel Cells That Like CO

The production of hydrogen from hydrocarbons for fuel cell applications also creates CO and CO_2. The CO is especially a problem because it poisons the fuel cell catalysts. It can be removed via the water-gas shift reaction, which creates CO_2 and additional hydrogen, but the reaction is slow. **Kim *et al.*** (p. 1280; see the news story by **Service**) now show that polyoxometalate (POM) compounds such as $H_3PMo_{12}O_{40}$ react in aqueous solution with CO in the presence of gold nanotubes. The reduced POM compounds can then be reoxidized at the fuel cell anode to generate electricity.

A Return on Investment

Humans often engage in cooperative activities, not only with family members and friends, but even with strangers. They do so in the expectation that generous behavior will be reciprocated, resulting in mutual gains, and that those who take but do not give will be sanctioned. How such behavior arose evolutionarily has been debated because the individual who metes out punishment usually incurs a cost without receiving a direct benefit. **De Quervain *et al.*** (p. 1254; see the cover and the Perspective by **Gutscher**) use brain imaging to show that in a game situation, the punisher does in fact enjoy the satisfaction of correcting violators of cultural norms. An individual who experienced a greater sense of satisfaction was willing to spend more money in order to punish the offender.

The Wheres and Hows of Memory

The hippocampus plays a fundamental role in encoding, consolidating, and retrieving episodic and semantic memory (see the Perspective by **Bilkey**). **Fyhn *et al.*** (p. 1258) show that precise spatial infor-

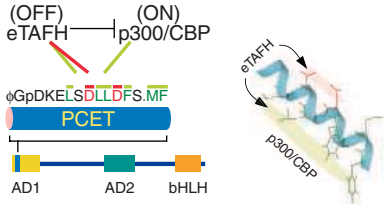
CREDITS: (TOP TO BOTTOM) SMITH *ET AL.*; WU *ET AL.*

mation exists and arises in neural activity upstream of the hippocampus in a hitherto unexplored dorsocaudal area in the medial entorhinal cortex, and that this information is being computed within this area. The entorhinal cortex may thus have the processing power to compute and represent position. To understand the functional differentiation underlying structural differences in the patterns of neuronal connectivity within the hippocampus, **Leutgeb *et al.*** (p. 1295, published online 22 July 2004) performed ensemble recordings in hippocampal areas CA1 and CA3 when rats were placed in varying enclosures in different recording rooms. The ensemble codes in CA3 were independently organized, whereas codes in CA1 overlapped one another, especially when the animals were placed in familiar-looking surroundings. The CA1 appears to register more general features, whereas CA3 appears to store overlapping but different memories with minimal interference.

Controlling GAS

The "flesh eating bacteria" group A streptococci (GAS, *S. pyogenes*) are responsible for sore throats, for complications of rheumatic fever and glomerulonephritis, and for necrotizing fasciitis. Like most microbial pathogens, the range of host species that can be infected by a particular GAS is highly restricted. **Sun *et al.*** (p. 1283) now find that this host target restriction relies on the highly specific interaction between bacterial streptokinase and host plasminogen. Mice expressing a human plasminogen transgene showed increased sensitivity and mortality to human GAS pathogens. In these mice, streptokinase activation of human-derived plasminogen facilitated blood clot dissolution and enhanced bacterial spread.

Gene Silencing in Leukemia?



About 15% of acute myeloid leukemia display a chromosomal translocation with high-level expression of leukemogenic AML1-ETO fusion proteins. AML1-ETO contains a conserved TAF4-homology domain (TAFH) for which in vivo function is unknown, but which might be expected to complex with other transcription factors. **Zhang *et al.*** (p. 1286) now show that the TAFH domain AML1-ETO, and nonleukemic factor ETO, associates with HEB protein, a transcription factor of the E protein family. The domain by which ETO interacts with E protein coincides with the site targeted by p300/CBP histone acetyltransferase. The association of HEB and ETO may sterically block p300/CBP recruitment in vivo and allow recruitment of negative co-factors such as HDACs for gene silencing of HEB-responsive promoters in leukemic cells.

Autophagy and Parkinson's Disease

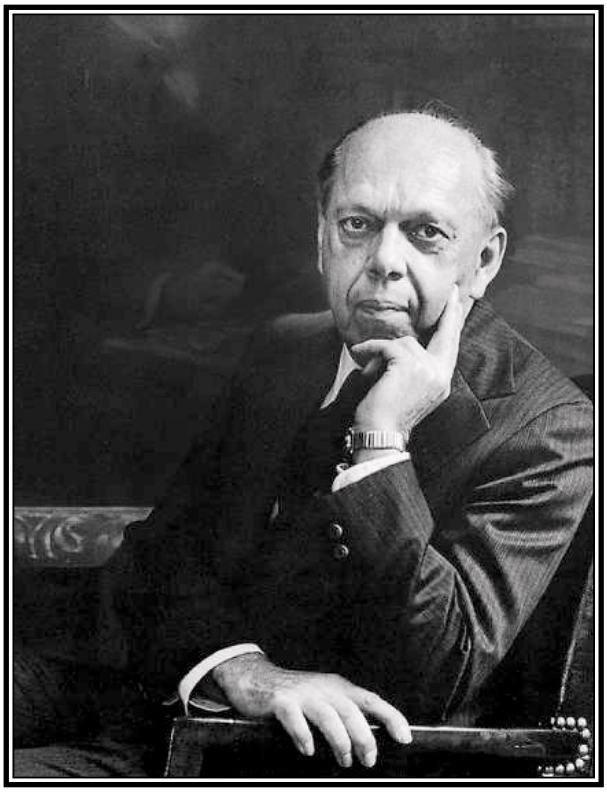
The cause of Parkinson's disease, the second most common neurodegenerative disorder, remains unknown. It is widely suspected that Lewy bodies, the intraneuronal signature of the disease, and perhaps neuronal death, result from aberrant degradation of synuclein, a protein that is known to play a role in the pathogenesis of Parkinson's disease. **Cuervo *et al.*** (p. 1292) now show that wild-type synuclein is degraded in lysosomes by chaperone-mediated autophagy. In contrast, the pathogenic synuclein mutants are not degraded, and actually block chaperone-mediated autophagy. This finding may explain the basis by which mutant synucleins cause familial Parkinson's disease.

Protecting the Genome?

In plants, the yeast *Schizosaccharomyces pombe*, and *Drosophila*, small interfering (si)RNAs that are generated as part of the RNA interference process can silence gene expression either posttranscriptionally, by the cleavage of homologous target RNAs, or transcriptionally, by inducing the formation of heterochromatin and/or the methylation of homologous DNA sequences. **Morris *et al.*** (p. 1289), published online 5 August 2004) now show that siRNAs can mediate transcriptional gene silencing in human cells when the siRNAs are delivered to the nucleus. siRNAs directed against gene promoter sequences result in methylation of the DNA. Transcriptional gene silencing probably plays a role in defending the genome from transposons and repeated sequences.

CREDIT: ZHANG *ET AL.*

IN MEMORY OF



PHILLIP HAUGE ABELSON
1913–2004

"Part of the strength of science is that it has tended to attract individuals who love knowledge and the creation of it."
Phillip Hauge Abelson, "The Roots of Scientific Integrity," Science, *1963*

The staff of AAAS and *Science* mourn the passing of Phillip Hauge Abelson — visionary scientist, respected leader, beloved colleague and friend.

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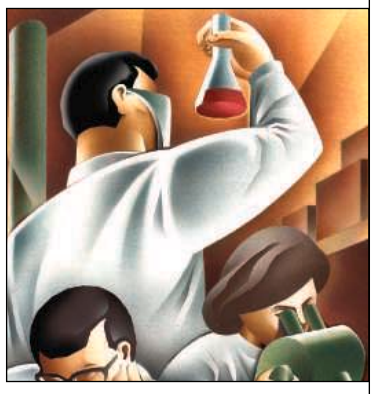
Academic Health II

I started this second diagnostic foray into the health of American universities with good intentions and a list of topics—but events intervened, as events often do. For example, an alarming postscript has been added to one of the issues discussed in last week's Editorial. The inspector general of the Department of Defense had produced a report urging contract officers to watch contract language more carefully (*Science*, 23 April 2004, p. 500). Two other agency inspectors general have since come out with ominously similar recommendations. It is uncertain how all this will be interpreted, but university administrators worry that the government will become more willing to attach restrictions short of classification to research awards, in the name of export control. Didn't anyone out there hear National Security Advisor Condoleezza Rice say that National Security Decision Directive (NSDD) 189 still held, and that we therefore weren't using halfway proxies for classification?

But another and even larger worry has also intervened. It now is becoming clear that the biggest problem in higher education in the United States is the steady erosion in the economic health of its great state-supported public universities. There was a time when these institutions dominated the sector. When William Rainey Harper became president of the University of Chicago in 1890, he described his fledgling but handsomely endowed institution as "surrounded by the great engines of public instruction." This politically adroit, poor-me bow to the Big Ten universities echoes strangely in 2004, when the faculty of the University of Illinois would surely like to have The University of Chicago's salary structure.



The economic decline of state budgets, of course, is largely responsible, and its sources have recently been analyzed in a 2003 Brookings Institution study by Thomas Kane and Peter Orszag. There are a variety of causes: business cycle effects influencing tax revenue and—most important—the escalation of Medicaid costs. The expected result in state appropriations for higher education is that these have dropped from about $8.50 per $1000 in personal income in 1977 to about $7.00 in 2003. The resulting changes in faculty salaries and other indicators of academic welfare, as documented in the Kane and Orszag study, are these. First, state spending per student in public institutions versus private ones fell from 70% in 1977 to 58% in 1996. Second, there has also been an adverse effect on student recruitment, as candidates in the highest categories of the usual admissions criteria have increasingly preferred private to public universities. Finally, and perhaps most troublesome, faculty satisfaction in the public universities has also dropped. Small wonder: In 1981, the ratio of public to private university professorial salaries stood right about at parity; by 2000, it had dropped to about 0.85.

The struggle for the public universities, as they labor at the low end of this tilted playing field, is increasingly desperate. Some, like the universities of Virginia and Oregon, have adopted a "privatization" strategy, upping tuition (especially for out-of-state students) to make up for shrinking state allocations—which, in many institutions, now constitute less than 15% of total revenues. The University of California has limited enrollment by requiring otherwise-qualified applicants to attend community colleges for 2 years. Research has also suffered, although formula funding for agricultural research has left the land-grant institutions in somewhat better shape than the others.

What is to be done? The academic community, especially its private sector, needs to be aware of the situation and support the public universities wherever state or national policies are being crafted. Federal policies could make a difference by reforming Medicaid—the key factor in driving out state higher education support. As for the states, they need to recognize what a powerful economic engine higher education represents, and consider the long-term costs of failing to fuel it. A final possibility, surely the most politically controversial, arises because most state institutions provide a large educational subsidy in the form of tuition charges for all students that are way below the real cost of education. Unlike other state welfare programs, this comes with no means test. If families who can afford the real cost of education had to pay something closer to it, the new revenue could be applied to financial aid for able but poor candidates—leaving something over for program improvement. It's an unpopular idea, but in hard times it may belong on the table.

Donald Kennedy
Editor-in-Chief

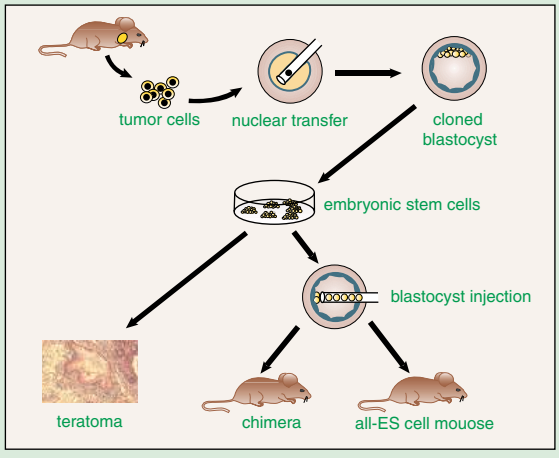
edited by Gilbert Chin

CANCER

Reprogramming Cancer Cells

An anguished Lady Macbeth says, "What's done cannot be undone." Does this apply to cancer cells?

Cancer arises as a result of both genetic and epigenetic modifications. Whereas genetic changes permanently alter the DNA sequence of the tumor cell, epigenetic changes act more subtly—for example, by altering the way that critical proteins are packed around DNA. The extent to which these reversible epigenetic changes contribute to tumorigenesis is poorly understood.



Procedure for assessing the tumorigenic potential of ES cells.

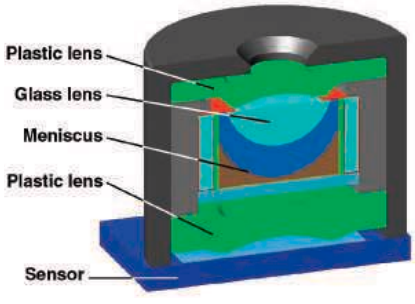
In two studies, investigators have examined whether cancer cells can be reprogrammed into a normal state by transferring nuclei from mouse tumor cells into enucleated mouse oocytes and then assaying their ability to direct early embryo development. Blelloch *et al.* found that transfer of nuclei from embryonal carcinoma cells resulted in normal blastocysts from which embryonic stem (ES) cells could be produced, but the ES cells had the same tumorigenic potential as the donor cells. Hochedlinger *et al.* likewise found that nuclei from many tumor cell lines could not be reprogrammed. One remarkable exception, however, was a melanoma cell line whose nucleus not only produced ES cells, but was able to direct the full development of an adult mouse. These results underscore the important role of genetic changes in tumor development, but raise the possibility that in certain tumor types, epigenetic changes may play a predominant role. — PAK

Proc. Natl. Acad. Sci. U.S.A. 10.1073/pnas.0405015101 (2004); *Genes Dev.* **18**, 1875 (2004).

APPLIED OPTICS

A Liquid Lens

Mechanical imaging systems focus images by using tiny motors and drivers to position the lens physically. The miniaturization of mechanical systems requires precision engineering and is limited by the tolerances of the machining tools. Kuiper and Hendriks demonstrate that the meniscus, or curvature, of the interface between two immiscible liquids can be controlled by application of an electrostatic potential. They go on to show that this effect can be used to instantiate a variable focus lens by building a miniature camera suitable for incorporation into a mobile phone. Without any moving parts, the liquid lens should find immediate application in a wide range of optical devices where size, speed, and robustness are critical requirements. — ISO



Schematic of the liquid lens

Appl. Phys. Lett. **85**, 1128 (2004)

MATERIALS SCIENCE

Silicon Windows

Although the sample chambers in most electron microscopes are under vacuum, environmental scanning electron microscopes are making it feasible to analyze biological samples at ambient pressures. For these microscopes to work, the electron column, where the beam is formed, has to stay under high vacuum, and so a cascade of pressure stages (like a series of locks in a canal) is used to maintain a pressure gradient. Similarly, if x-ray detectors are used, they need to be protected from contamination with a window made either of beryllium, which cuts off x-rays below 1 keV, or of a polymer, which can be fragile.

Schilling *et al.* have fabricated a macroporous silicon membrane using photoelectrochemical etching to generate the pores, followed by oxidation and chemical etching to smooth them out. The resulting structure features 50-μm-long pores that are capped with dome-shaped silicon dioxide shells, only 60 nm thick. The nonporous regions of the membrane allow it to withstand a pressure differential of ambient on one side and vacuum on the other. Transmission levels for an electron beam with an accelerating voltage of 25 keV were as high as 22%, albeit with significant variation from pore to pore. Further tests showed that these membranes would also transmit x-rays and infrared radiation. — MSL

Appl. Phys. Lett. **85**, 1152 (2004).

IMMUNOLOGY

Sharing with the Needy

When not responding to pathogens, naïve T cells survive with the aid of a variety of homeostatic influences. Dominant among these is the signal provided by the cytokine interleukin-7 (IL-7), which maintains the activity of anti-apoptotic (anti-death) pathways. However, the limiting amounts of IL-7 that are available relative to the large number of T cells suggests that a mechanism must exist that enables cells to compete successfully for this resource without risking the loss of antigenic diversity as represented by the whole T cell population.

Park *et al.* observed that expression of the IL-7 receptor (IL-7R) was reduced on T cells that had already received an IL-7 signal. This was traced to a decrease in transcription of the gene encoding the α chain of the IL-7R and was ascribed to activation of the transcriptional repressor GFI1. In transgenic mice with forced constitutive expression of the IL-7R α chain the T cell pool was reduced, rather than expanded,

CREDITS: (TOP) HOCHEDLINGER ET AL., *GENES DEV.* **18**, 1875 (2004); (BOTTOM) KUIPER AND HENDRIKS, *APPL. PHYS. LETT.* **85**, 1128 (2004)

indicating that prolonged IL-7R expression in these animals had conferred an overall survival disadvantage. Thus, the survival benefit of IL-7 is spread across the pool of naïve T cells by reducing demand from those T cells that have already received their allotment: an efficient means by which cells share a scarce resource. — SJS

Immunity **21**, 289 (2004).

ASTROPHYSICS

Denuded Dwarfs

Globular clusters of stars are ubiquitous and provide important clues about galaxy formation. They also are large and luminous, and hence one of the easier kinds of sub-galactic objects to study. They all "look" the same; that is, they have scale radii, surface brightness, and velocity dispersion properties that are similar from one globular cluster to the next, suggesting that they all formed in the same fashion. But how do millions of stars come together into a relatively featureless glob?

Martini and Ho observed 14 new globular clusters in a large elliptical galaxy, Centaurus A, and estimate that these clusters are almost as massive as dwarf galaxies. In fact, the clusters have properties so similar to those of the centers of dwarf galaxies that the authors conclude the clusters might actually be the naked cores of dwarf galaxies. In other words, these shapeless clusters might once have been beautifully structured galaxies that were tidally stripped of their finery. Such a reclassification would alter hierarchical models of galaxy formation and enhance the importance of near-collisions between galaxies that lead to tidal stripping. — LR

Astrophys. J. **610**, 233 (2004).

ECOLOGY/EVOLUTION

Maintaining One's Niche

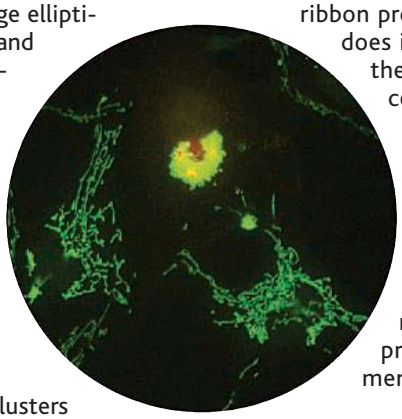
The concept of limiting similarity—literally, the limits to how similar two species can be if they are to coexist in a habitat—is an important element in the theory of assembly rules governing composition and diversity within ecological communities. Nevertheless, rigorous empirical evidence for limiting similarity has been hard to obtain. Stubbs and Wilson, in a study of a sand dune plant community in New Zealand, examined whether plants with similar functional characteristics (such as height, leaf shape, root morphology, nitrogen and phosphorus content of leaves) coexisted less often than would be expected if their distribution were random. Plants were sampled at different spatial scales up to 50 m^2. Many of the functional characters showed less-than-expected mean dissimilarity at the 0.5 m^2 scale, providing support for the rule of limiting similarity in this community. The effects were seen particularly clearly in functional characters relating to nutrient uptake and the control of leaf water. — AMS

J. Ecol. **92**, 557 (2004).

CELL BIOLOGY

Ribbons and Bows

The Golgi complex in mammalian cells resides in a juxtanuclear position that depends on the centrosome and on microtubules. How is this single Golgi ribbon produced, and how does it "know" to form at the periphery of the centrosome? Rios *et al.* find that the protein GMAP-210, peripherally associated with cis- (the side facing the nucleus) Golgi membranes, binds to microtubules and promotes the recruitment of γ-tubulin–containing complexes to the Golgi. Reduction of GMAP-210 levels causes the fragmentation of the Golgi complex and interferes with membrane traffic. The ability of GMAP-210 to recruit organelles to the centrosomal region can be transferred—when GMAP-210, or only its C-terminal domain, was engineered to insert into the mitochondrial membrane, the mitochondria recruited γ-tubulin and moved toward the centrosome. Thus, GMAP-210 appears to play an organizing role in the generation and maintenance of a single, central Golgi complex. — SMH



Colocalization of mitochondria (red) and the engineered GMAP-210 C-terminal domain (green).

CREDIT: (RIOS *ET AL.*, *CELL* **118**, 323 (2004))

Cell **118**, 323 (2004).

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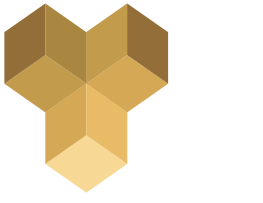

YOUNG SCIENTIST AWARD

NEW NAME NEW DEADLINE
SAME GREAT PRIZE!

The Amersham Biosciences, now part of GE Healthcare, and *Science* Prize for Young Scientists has changed its name to the Young Scientist Award.

PPROACH
D ENEMY

Cancer continues to be a major cause of death worldwide. Finding a cure is a key task for science, but the disease has proved an elusive enemy. Dr. Matthew Albert is a scientist who has taken up the challenge – and he is approaching it from an unusual angle.

While the mainstream approach is to study patients with cancer, Dr. Albert is looking at individuals with tumor immunity. His aim is to understand the mechanisms for this and find ways to reproduce them in people whose cancers have evaded the immune system. The discovery of a mechanism by which the immune system can mount an immune response against tumors led him to his latest research focus on how the immune system captures information from dying tumor cells.

Dr. Albert became a regional winner of the 2001 Prize for Young Scientists with an essay based on his Ph.D. research in this area at The Rockefeller University. He went on to join the Pasteur Institute in Paris as director of research at INSERM – becoming one of the youngest in France to hold such a position. He says, "The prize has been very important for me personally. It has put me in touch with a global community of scientists and led to valuable interactions. It also gave me added confidence to continue pursuing a line of research that fascinates me."

YOUR OPPORTUNITY TO WIN IS NOW

The Young Scientist Award was established in 1995 and is presented by *Science*/AAAS and GE Healthcare (formerly Amersham Biosciences). The aim of the prize has been to recognize outstanding Ph.D. graduate students from around the world and reward their research in the field of molecular biology.

This is your chance to gain international acclaim and recognition for yourself and your school. If you completed your Ph.D. in molecular biology* during 2003, describe your work in a 1,000-word essay. Then enter it for the **2004 Young Scientist Award**. Your essay will be reviewed by a panel of distinguished scientists, who'll select one grand prize winner and up to seven other winners. The grand prize winner will get his or her essay published in *Science*, receive US$25,000, and win a trip to the awards ceremony in Washington, D.C. The closing date for entries is **October 8, 2004**.

Go to **www.aaas.org/youngscientistaward** to find the entry form and award rules. We wish continued success to Dr. Albert. And to you.

Read Dr Albert's latest findings in *Nat. Rev. Immunol.* Mar. 4(3):223-31 2004.

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Science AAAS

GE imagination at work

* For the purpose of this prize, molecular biology is defined as "that part of biology which attempts to interpret biological events in terms of the physico-chemical properties of molecules in a cell" (*McGraw-Hill Dictionary of Scientific and Technical Terms*, 4th Edition).

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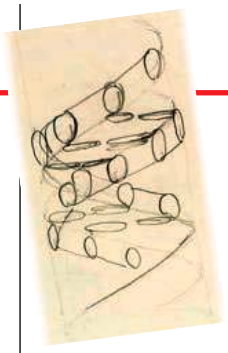


EXHIBIT

Crick Sampler

Francis Crick, who died last month, co-discovered the double helix and helped shepherd the field of molecular biology through its youth. You can peruse a selection of his early manuscripts, letters, notebooks, and photos at The Crick Papers from Britain's Wellcome Trust. The exhibit includes gems such as a draft of the 1953 paper that elucidated DNA's structure and the 1962 telegram informing him of his Nobel Prize. (Above, a 1953 sketch of the double helix.)

www.wellcome.ac.uk/en/genome/geneticsandsociety/hg13f012.html

RESOURCES

You Can Get There From Here

Although its name conjures up fallen arches and jet lag, the traveling salesman problem (TSP) is a mathematical conundrum that requires calculating the cheapest route among a selection of cities. The problem intrigues mathematicians because it can provide insight into theoretical questions and help with a host of practical puzzles, from manufacturing microchips to mapping the genome. Uncover more at Solving TSPs, hosted by Georgia Tech University in Atlanta. Newbies can trace the idea's development—its origins are uncertain, but it inspired a parlor game in the 1800s—or peruse images of famous or attractive shortest routes. Experts will find free software for cracking problems. In background, the optimal route for visiting 666 of the world's most famous sights.

www.tsp.gatech.edu/index.html

DATABASE

The Science of Supplements

Research on the safety and effectiveness of dietary supplements is more plentiful than you might think, judging from this refurbished site from the National Institutes of Health. Aimed at researchers and the public, the database supplies titles and in most cases abstracts for more than 730,000 studies, news articles, and other publications. For example, you'll find more than 160 entries on the weight-loss preparation ephedra, which the Food and Drug Administration recently banned because it can trigger heart attacks and strokes.

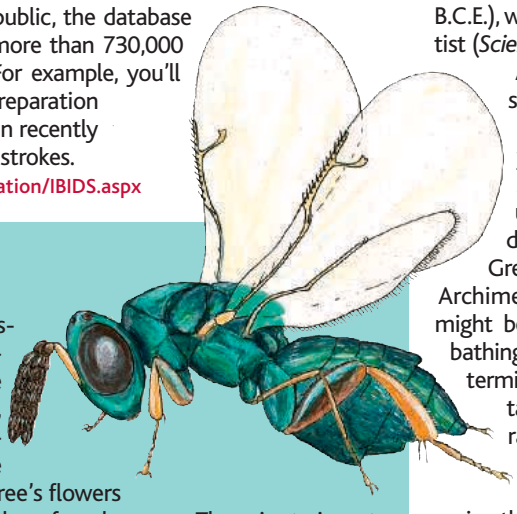
dietary-supplements.info.nih.gov/Health_Information/IBIDS.aspx

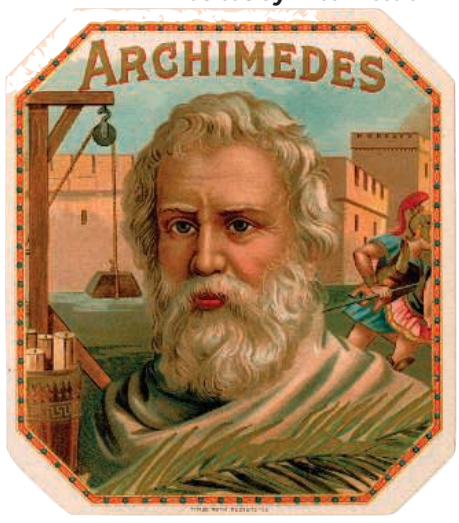
EDUCATION

Home Sweet Home

The wasp and the fig tree isn't one of Aesop's lesser-known fables, it's the true story of an interkingdom partnership essential for producing the tasty fruit. Discover the details of this intricate, reciprocally beneficial relationship—what ecologists call a mutualism—at this site from the Iziko Museums in Cape Town, South Africa. The tree's flowers are tucked inside the fig, whose alluring scents draw female wasps. The minute insects wriggle into the fruit's interior, where they lay their eggs and pollinate the flowers. Newly hatched wasps munch on the fig then fly away, carrying pollen to another tree. The site features photos and artwork illustrating fig and bug adaptations. Cheaters can prosper in this situation—this species of *Otitesella* (above) injects its eggs into the fig without spreading pollen.

www.figweb.org





EXHIBIT

The First Eureka Moment

Historians usually rank Archimedes as one of the three greatest mathematicians for achievements from refining estimates of pi to laying the groundwork for calculus. This archive from Chris Rorres, an applied mathematician at the University of Pennsylvania in Philadelphia, brims with lore and trivia about Archimedes (circa 287 B.C.E.–212 B.C.E.), who was also an engineer and scientist (*Science*, 20 August, p. 1102).

Animations and reconstructions show how some of his devices might have worked. For example, you can study the mechanics of Archimedes' claw, a huge crane for upending enemy ships designed to defend his home of Syracuse, a Greek city-state. As the site relates, Archimedes' most famous "discovery" might be apocryphal. He was supposedly bathing when he figured out how to determine if the king's golden crown contained silver; thrilled, he reportedly ran through the streets naked shouting, "Eureka!" Scholars, however, note that his solution—comparing the volume of water displaced by the crown and by an equal mass of pure gold to see if they had the same density—doesn't display his usual creativity and would have required precise measurements hard to obtain at the time.

www.math.nyu.edu/~crorres/Archimedes/contents.html

Send site suggestions to netwatch@aaas.org. Archive: www.sciencemag.org/netwatch

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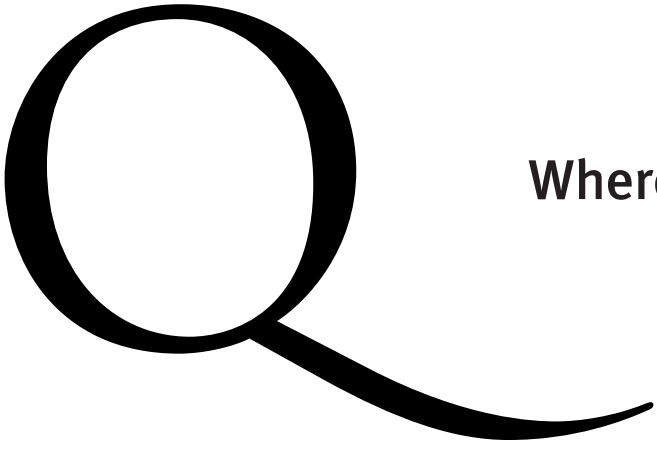

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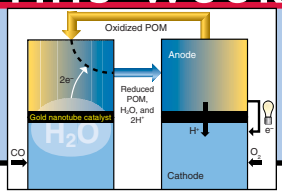
NEWS

This Week



PAGE 1225
A friendlier fuel cell

1226
Patented advocacy

PHARMACOGENOMICS

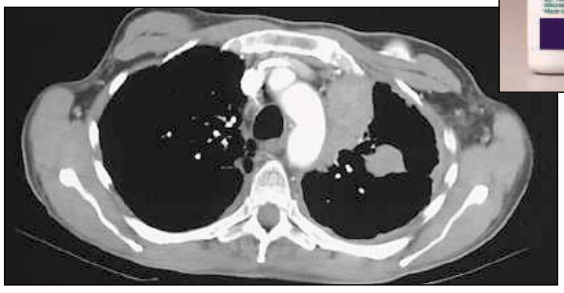
Cancer Sharpshooters Rely on DNA Tests for a Better Aim

Without fanfare, two diagnostic labs have launched a genetic test to guide doctors treating a common and deadly form of lung cancer. Despite lingering questions about whether the test is comprehensive, physicians think this approach could herald a new generation of gene-based methods of tailoring cancer treatment.

Designed to pinpoint patients who might be helped by the drug Iressa, the new test hunts for mutations in a gene called *epidermal growth factor receptor* (*EGFR*), whose protein Iressa targets. People who test positive may be more likely to benefit from this therapy, which has an impressive record in treating non–small cell lung cancer—but only in a small fraction of cases. If screening takes off, it could significantly affect the roughly 140,000 U.S. patients diagnosed each year with this type of cancer.

This month, a Harvard-affiliated diagnostics lab rolled out its version of the Iressa test, following a similar decision in July by the City of Hope hospital in Duarte, California. Both offer similar tests to lung cancer patients (at a cost of $500 to $2000), screening for mutations in DNA isolated from tumors.

Approved by the U.S. Food and Drug Administration in May 2003, Iressa initially baffled doctors with variable results: Tumors shrank in only about 10% of patients, but in that group the response was dramatic. Researchers concluded that the drug worked best in those with EGFR-dependent tumors, but there was no way to identify such patients. That became possible last spring, when two independent teams of scientists at Massachusetts General Hospital (MGH) and the Dana-Farber Cancer Institute, both in Boston, reported that Iressa responders have mutations in a specific stretch of the *EGFR* gene (*Science*, 30 April, p. 658).



Genetic forecasting. Doctors hope a new gene test will help them pick and choose patients whose lung tumors (above, right) are most likely to shrink thanks to the targeted drug Iressa.

"Hundreds of patients have contacted us" to learn their *EGFR* status, says Thomas Lynch, who directs the center for thoracic oncology at the MGH cancer center and was a lead author on one of the spring papers. Adds Matthew Meyerson, a pathologist at Dana- Farber and an author of the second paper: "Our goal, basically, is to get the test into the widest and fastest possible use."

But the details must be ironed out. For one, the research groups are not equipped to handle the hundreds of thousands of samples that could flood in. (So far, each has tested fewer than 20.) "We're hoping there will be a commercial test," says Lynch, adding that MGH and Dana-Farber have applied for patents and are discussing this with "more than one company." The current goal, says Daniel Haber, head of the cancer center at MGH, is to sign on a company willing to distribute the genetic test to hospitals that want to screen their own patients. "We are not looking at the model Myriad has," he says, referring to Myriad Genetics, the Salt Lake City, Utah, company whose monopoly over two breast cancer gene tests has spurred controversy. ▶

U.S. VISA POLICY

Foreign Scholars to Get Longer Clearance

The United States plans to extend the validity of security clearances for foreign students and scientists beyond the current 1-year duration. The new policy, which government officials say could be implemented as early as this fall, will reduce delays for U.S.-based international scholars seeking to reenter the country.

"We've heard loud and clear from the university and scientific communities that the image of this country as a venue for research and scholarship has been suffering," says C. Stewart Verdery Jr., assistant secretary for border and transportation security policy at the Department of Homeland Security (DHS). "And we want to change that."

Foreign students and researchers who work in sensitive fields of science and technology currently must undergo a security review to obtain a reentry visa if their last clearance was granted more than 12 months ago. Under the new policy, which has yet to be finalized, the clearance could be valid for as long as the duration of their study or academic appointment. DHS officials say the extension is a result of improved measures to monitor individuals entering and leaving the country. Through the Student and Exchange Visitor Information System, for instance, "we can know when an international student majoring in English has switched to nuclear engineering," says Verdery. "And if the system shows that a scholar is returning for the same activity that he or she was pursuing prior to leaving the U.S., it makes sense not repeat a security check."

The administration is also planning to revise the list of sensitive technologies used to determine whether a visa applicant needs to undergo an elaborate interagency review. DHS officials say that the department will consult with scientists to review the list, which they acknowledge is "too broad."

The scientific community sees the proposed changes as the latest in a series of positive steps. "They've already made some serious efforts to minimize visa delays," says Mark Frankel of AAAS, publisher of *Science*, which this spring helped draft a set of visa policy recommendations (*Science*, 14 May, p. 943).

–YUDHIJIT BHATTACHARJEE

CREDITS: (TOP TO BOTTOM) ASTRAZENECA; ROY HERBST/M. D. ANDERSON CANCER CENTER

1228
Sniffing out danger

1231
Visionary in a hurry

1235
Not just for sport

In addition, new biological complexities are appearing: Preliminary studies have identified patients who respond to Iressa but who don't have *EGFR* mutations in the DNA swath tested. Vincent Miller, a thoracic oncologist at Memorial Sloan-Kettering Cancer Center in New York City, is concerned that some patients who could benefit from Iressa might not receive it after testing negative.

One possibility is that relevant mutations may be hiding elsewhere in the *EGFR* gene. Based on that hypothesis, says the chief of the clinical molecular diagnostic lab, Steve Sommer, the City of Hope has just launched a second *EGFR* test that screens the entire *EGFR* gene. That's four times as much DNA as the Boston test and the original City of Hope test cover.

Meanwhile, several hospitals, led by MGH, are planning a clinical trial for October to better correlate mutations with drug responses. The trial will enroll 30 newly diagnosed lung cancer patients with *EGFR* mutations and offer them Iressa up front.

Physicians are already beginning to extend findings from Iressa studies to a related drug, Tarceva, which also targets *EGFR*. Early studies show that the same mutations may help determine the success of Tarceva therapy.

–JENNIFER COUZIN

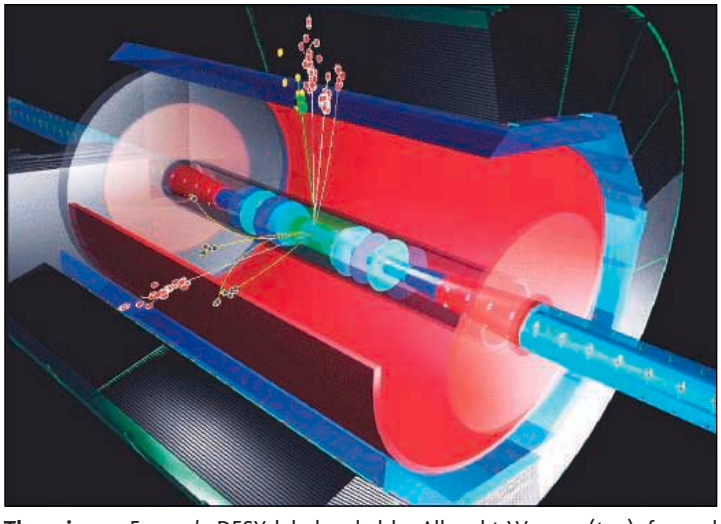
NEXT LINEAR COLLIDER

Physicists Pick a Cold Road for Accelerator Project

Particle physicists are hot to trot with a cold linear collider. Although money and politics may prevent it from ever being built, the next big machine to explore the fundamental forces and particles in the universe should use "cold" superconducting technology rather than "warm" traditional conductors, scientists decided last week. "It's a very important point," says Jonathan Dorfan, director of the Stanford Linear Accelerator Center (SLAC). "We will all come together now, enthusiastically, to come to a design."

A more powerful linear collider is the next logical step in a 75-year sequence of building particle accelerators. In 2007 or 2008, the Large Hadron Collider (LHC) at Europe's CERN lab near Geneva, Switzerland, will begin to search for new particles. Most particle physicists have high hopes that the LHC will discover important exotica such as the Higgs boson and "supersymmetric partners" of known particles. But the LHC, which smashes complicated protons together, won't have the finesse to analyze those discoveries in detail. A linear collider, which smashes simple electrons and antielectrons together, can be used to figure out the properties of the new particles with greater precision.

At a Colorado summit in 2001, particle physicists across the United States agreed to pursue a next-generation linear collider (*Science*, 27 July 2001, p. 582), but they split over how to accelerate the electrons and antielectrons to smashing speed. Scientists at Japan's KEK laboratory in Tsukuba and at SLAC favored using copper cavities to pump an extremely large amount of energy into the accelerating particles in a relatively small space. The European DESY lab in Hamburg, Germany, meanwhile, championed a plan to use superconducting niobium cavities to accelerate the electrons and antielectrons in a more leisurely—but more efficient—manner. "Warm technology supports a higher gradient, so you can get a physically smaller, shorter machine," says Stephen Holmes, associate director for accelerators at the Fermi National Accelerator Laboratory in Batavia, Illinois. "Cold technology uses less power, so it's cheaper to operate."



The winner. Europe's DESY lab, headed by Albrecht Wagner (*top*), favored superconducting technology it developed for its TESLA collider (*bottom*).

Most scientists agreed that either technology would have done the job well at about the same cost. Paul Grannis, a particle physicist at the State University of New York, Stony Brook, and a member of the panel that made the choice, says that several factors played crucial parts in the decision. For example, the lower-frequency operation of the cold technology makes it somewhat less sensitive to problems such as ground motion, Grannis says. The technology is also similar to that which DESY's Tera-electron-volt Energy Superconducting Linear Accelerator (TESLA) collaboration developed for the lab's planned X-FEL free-electron laser project, which will help pave the way for the superconducting collider (*Science*, 10 May 2002, p. 1008).

Physicists' consensus boosts the accelerators' prospects, says DESY's project leader for linear collider research, Rolf-Dieter Heuer: "This is what politicians want—a clear view of how to proceed. It brings us to a very strong position."

The next step is to come up with a conceptual design for the machine, a task that should take 2 years or so. "I don't have a good answer" for costs, says Dorfan. "But it will be many billions of dollars."

–CHARLES SEIFE

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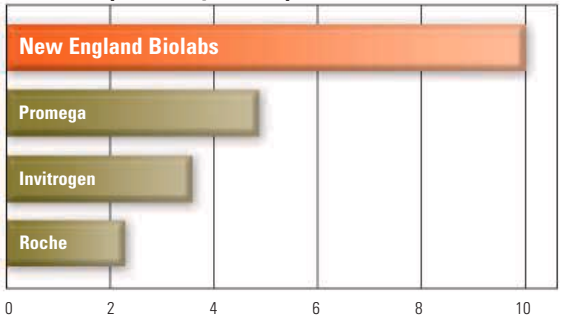

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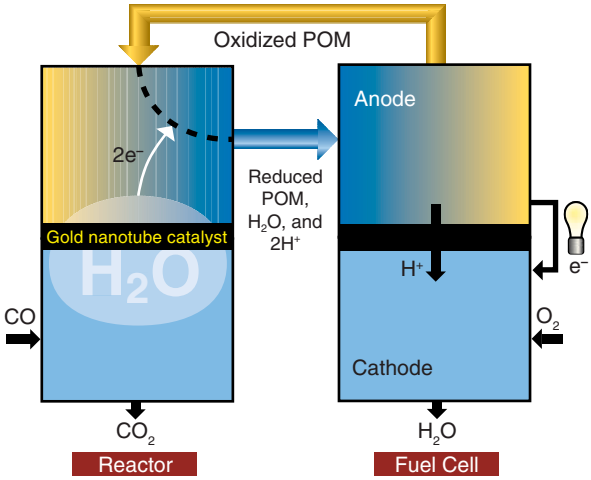
CHEMISTRY

Fuel Cell Draws Power From Poison

Scientists working on automotive fuel cells have come up with a way to turn a molecular adversary into a friend.

Low-temperature fuel cells use platinum catalysts to extract electricity from hydrogen gas. But when that gas is produced from fossil fuels—the most common source—it's invariably contaminated with carbon monoxide (CO), which poisons the catalysts. On page 1280, however, researchers led by chemical engineer James Dumesic of the University of Wisconsin, Madison, report that they've solved the problem and, for good measure, created another source of fuel.

"It's pretty novel and interesting," says Matthew Neurock, a catalysis expert at the University of Virginia, Charlottesville. Neurock and others say the work might help make fuel cells cheaper by scrapping part of the high-temperature apparatus currently required to eliminate CO from hydrogen fuel. It could also be welcome news for those who advocate generating hydrogen fuel from renewable fuels such as agricultural waste, because producing hydrogen from "biomass" also produces large amounts of CO. "This opens the door to using renewable energy resources," Neurock says.



Interception. Aided by a stream of electron-ferrying polyoxometalates, a gold-catalyst reactor strains out carbon monoxide that could otherwise wreck a fuel cell.

Makers of low-temperature fuel cells—called polymer electrolyte membrane (PEM) fuel cells—currently fight their molecular enemy by sending their fuel through an initial chamber where CO reacts with vaporized water at temperatures of 500°C or more. At this high temperature, CO molecules grab oxygen atoms from water molecules to make carbon dioxide (CO_2), an inert gas that's vented to the air. The leftover hydrogen joins the rest of the hydrogen gas that's fed to the fuel cell.

The process cleans up fuel effectively. But it's costly and inefficient to create the high temperatures needed for the reaction and then cool the exhaust gases below 100°C, as most low-temperature fuel cells require, says Robert Hockaday, founder of Energy Related Devices, a fuel cell maker in Los Alamos, New Mexico.

Earlier this year, Dumesic's team found a cool alternative: a membrane coated with gold nanotubes and nanoparticles. On the nanoscale, Dumesic explains, normally unreactive gold becomes so active that it catalyzes reactions swiftly even at low temperatures. For their current study, Dumesic, postdoctoral assistant Won Bae Kim, and students Tobias Voitl and Gabrielle Rodríguez-Rivera used their nanogold catalyst to react CO and liquid water to create CO_2, hydrogen ions (H^+), and electrons (e^-). Instead of letting the energy in the electrons fizzle away, they captured it with electron-ferrying "redox" compounds known as polyoxometalates (POMs) dissolved in the water surrounding the membrane. POMs carry a strong positive charge that makes them hungry for electrons. When those electrons bind to the POMs, they turn the solution from a bright yellow to a vivid deep blue.

To recover the energy from the electron-toting POMs, Dumesic's team piped the solution, mingled with hydrogen ions from the CO reaction, to the front end of a PEM fuel cell. There, a positively charged electrode—the anode—stripped off the electrons and turned them into usable current. The oxidized POMs were then recycled to the gold-nanotube reactor to convert more CO. The rest of the process—combining the hydrogen ions, electrons, and oxygen at the cathode to create water—was standard fuel-cell chemistry.

The novel scheme for befriending CO is getting mixed reviews. Shimshon Gottesfeld, chief technology officer at MTI Micro Fuel Cells in Albany, New York, notes that fuel cells that ferry electrons by means of chemicals such as POMs are typically less efficient than devices that move electrons using electrodes. But Hockaday likes the way the system cleans up hydrogen fuel, and he and others predict that industry will be interested. "I would use it," he says.

–ROBERT F. SERVICE

SOURCE: ADAPTED FROM W. B. KIM *ET AL.*, *SCIENCE*

ScienceScope

Plum Island Breaches Assailed

Officials at a federal biosafety lab on Plum Island in New York are beefing up security procedures after six animals inadvertently became infected with foot-and-mouth virus this summer. Although the animals were within the biocontainment area, the cases, which became public last week, have added to concerns that such accidents may become more common as biodefense research expands.

The incidents occurred at the Plum Island Animal Disease Center on Long Island, a biosecurity level (BSL) 3 facility that is overseen by the Department of Homeland Security (DHS). On 24 June, two cattle were found to be infected with a virus strain being used in a separate part of the lab, says DHS spokesperson Donald Tighe. About 4 weeks later, four pigs in a clean room were discovered to be infected with a different strain.

DHS officials informed local activists soon after the second incident. But in a 2 August letter, Senator Hillary Rodham Clinton (D–NY) and Representative Timothy H. Bishop (D–NY) called the infections "alarming breaches." Virologist Frederick Murphy of the University of California, Davis, says that although such accidents aren't surprising, they suggest a "serious need" to review safety. Lab officials say they have implemented new procedures, such as an extra decontamination shower for workers and additional equipment sterilization, to avoid future problems.

–JOCELYN KAISER

Poll Shows Voters Split on California Stem Cell Initiative

A California ballot initiative to raise $3 billion for stem cell research is ahead in a recent poll—but that may not be enough to ensure victory. A 15 August Field Poll of 1034 Californians found that 45% of likely voters supported Proposition 71, which would create the California Institute for Regenerative Medicine and authorize the sale of bonds to fund research. Forty-two percent oppose the measure and 13% are undecided. The poll had a margin of error of ±4.5%.

Democrats favor the proposition by a 2–1 margin, whereas Republicans are opposed by roughly the same proportion. College graduates and those with a postgraduate education overwhelmingly favor the initiative, whereas voters with no more than a high school education are opposed.

If history is any guide, the divided electorate suggests that the proposition will fail, say California voting analysts. But proponents still have room to find new supporters, noting that the poll showed that just 40% of Californians were aware of the measure.

–DAVID MALAKOFF

GENETICS

Patient Advocate Named Co-Inventor On Patent for the PXE Disease Gene

In an apparent first, the lay leader of an advocacy group has been recognized as a co-inventor with four scientists on a gene patent. This is evidence, says Francis Collins, director of the National Human Genome Research Institute, of the increasing role patient groups are playing in research.

The work deals with a transporter gene, known as either *MRP6* or *ABCC6*, that causes a rare connective tissue disease called PXE (pseudoxanthoma elasticum). Sharon Terry, mother of two children with PXE and executive director of the group PXE International in Washington, D.C., is one of five inventors on a patent issued on 24 August by the U.S. Patent and Trademark Office. A diagnostic test should be available "by the end of the year," says Terry, and PXE International expects to offer it to its members by then.

Hands on. After her two children were diagnosed with a rare disease, Sharon Terry helped scientists find the responsible gene.

PXE is not usually lethal, but the calcium buildup it causes in certain cells can have devastating effects, such as vision loss, gastrointestinal bleeding, and heart disease. Harmful PXE gene mutations are thought to occur in 1 of about 50,000 people in the United States; there is no proven treatment. The four academic scientists listed as inventors of the PXE patent are members of a research collaboration led by Charles Boyd of the University of Hawaii, Honolulu. Although others had laid the groundwork for their studies, Boyd's group was first in a four-way race to publish 4 years ago (*Science*, 2 June 2000, p. 1565).

Sharon and her husband Patrick Terry founded PXE International 8 years ago and quickly helped mobilize support for scientific studies on an international scale. Genetic researchers often get help from families affected by rare diseases, for instance, in obtaining tissue samples and collecting family data. But Sharon Terry says she did much more: "I extracted DNA, ran gels, read the gels," and helped write the paper announcing the gene's discovery.

Collins says that Terry's direct contribution to the scientific work earned her a place on the inventor's list—a point subjected to "careful evaluation" by patent examiners. He views PXE International's involvement as a positive "example of how parents and lay organizations can play a catalytic role in research on rare diseases." Like many, he contrasts the PXE gene patent with the patent for the gene causing Canavan's disease; in that case, patient advocates sued a university and its scientist to regain control of a gene patent because they wanted to control testing costs and availability (*Science*, 10 November 2000, p. 1062). The lawsuit failed.

The success of PXE International, says Collins, has encouraged others. Leslie Gordon, mother of a child with a rapid-aging syndrome called progeria, worked with his lab in identifying a causative gene. A Ph.D.-pediatrician, Gordon is a co-author of the 2003 paper describing the progeria gene and one of the inventors listed on the patent application. She is also a co-founder and medical director of the Progeria Research Foundation in Peabody, Massachusetts.

Terry thinks PXE International may have to subsidize the price of gene testing, a typical use of which might be as a replacement for a painful skin biopsy to learn whether a younger sibling of a PXE patient is also at risk. It's a complex gene, difficult to analyze, she notes. After looking at DNA from 260 people, her group has found that six mutations account for 45% of the affected individuals. Capturing more mutations, and thus more of the affected population, may require additional DNA sequencing, which would be expensive.

"We're not sure how much it will cost" to test an individual, Terry says, but in some cases it could run to $3000 if it becomes necessary to sequence the entire gene. But whatever happens, Terry says, it's comforting to know that PXE International is now "driving the boat." **–ELIOT MARSHALL**

NUCLEAR WEAPONS POLICY

Showdown Expected in Congress

Take shelter, a political nuclear war is about to resume. An increasingly fiery debate over proposed new funding for U.S. nuclear weapons research and testing is expected to heat up again next month when members of Congress return from their summer recess.

At issue are three relatively small proposals that the Bush Administration included in its spending plan for the 2005 fiscal year, which begins on 1 October. One asks Congress to provide $27.6 million to develop an earth-penetrating nuclear weapon capable of destroying buried bunkers. The White House also wants $9 million to study "advanced concepts" for low-yield nuclear weapons and $30 million to shorten the time needed to prepare a site in Nevada if the United States were to resume underground testing of a nuclear weapon.

The White House argues that the moves are needed to enhance the country's ability to deter potential enemies and keep weapons scientists sharp (*Science*, 4 July 2003, p. 32). Administration officials insist that they have no plans to actually build or test new weapons, adding that Congress would have to approve those steps. But a bipartisan group of critics is skeptical, saying the proposals threaten to spark an expensive new arms race—even as the United States is seeking to prevent Iran, North Korea, and other nations from developing atomic weapons. "Each side gets to stress themes that resonate with its [political] base," says Jonathan Medalia, a national defense specialist at the Congressional Research Service in Washington, D.C.

Last year, the two sides fought to a draw, with Congress giving the White House approval to move ahead with the research but approving only about half of the requested funds. This year, the critics have already won the first round. In June, the full House of Representatives approved a Department of Energy (DOE) spending bill that eliminates funding for the three programs, even though the programs were authorized in separate measures approved by each house this summer.

In a harshly worded report that accompanied the spending bill, the House appropriations panel that oversees DOE said it was "unconvinced by [DOE's] superficial assurances" that the earth penetrator—which the White House says would cost nearly $500 million to develop—"is only a study and that advanced concepts is only a skills exercise for weapons designers." A leaked DOE memo, the panel charged, "left little doubt that the objective of the program was to advance the most extreme new nuclear weapon goals." Representative David ▶

CREDIT: GENETIC ALLIANCE

Hobson (R–OH), who heads the House spending panel, boasted in a recent public forum at the National Academy of Sciences on nuclear nonproliferation that he would "beat 'em again" if the White House tried to force another House vote on the issue. "I think they can count [votes]," he said.

The action now turns to the Senate, which has traditionally been friendlier to the three programs and has already defeated several efforts to eliminate them. Its version of the DOE spending bill could come to a preliminary vote as early as next month. If it approves funds for the programs, a House-Senate conference committee would have to settle the issue. Campaign politics could delay any final decision until after the November elections. **–DAVID MALAKOFF**

PRIMATE STUDIES

Politics Derail European Chimp Home

A battle over where to build a permanent retirement home for Europe's last remaining research chimpanzee colony is intensifying. Plans for a facility in Spain were derailed this spring, when the mayor of the tiny Spanish mountain town slated to host it declared his opposition to the project. Now, the Dutch charity that plans to build it has launched an international campaign to salvage the project.

The search for a final home began in 2002, when the Netherlands banned the use of chimps in research. Under pressure from animal-rights groups, the Dutch government agreed to take 63 remaining chimps away from the Biomedical Primate Research Center in Rijswijk by mid-2005 and hand them over to Foundation AAP, which runs a private primate shelter. At its Almere headquarters, AAP plans to build a permanent home for 30 chimps infected with hepatitis C and the simian cousin of HIV. For 33 uninfected chimps, however, it bought a 45-hectare estate in Relleu, near Alicante on Spain's eastern coast, where they can live more comfortably and cheaply than in the Netherlands. The facility would also house other abandoned and confiscated primates from all over Europe.

Chimp champion. Jane Goodall showed her support for a primate retirement center by planting a "tree of hope" at the proposed site on 14 July.

CREDIT: FOUNDATION AAP

In 2002, Relleu's elected mayor, Santiago Cantó, signed a letter supporting the facility, saying it would benefit the local economy with minimal environmental impact. But last March, Cantó reversed himself and asked the regional government not to issue a "declaration of public interest," a key bureaucratic hurdle. Any economic benefits were irrelevant, Cantó wrote, given the "social unrest" that the plans had caused. He cited the risk of noise, odors, and zoonotic diseases and said the facility would hurt tourist development at nearby properties. Although it has supported the plans, the regional government is unlikely to overrule the mayor's opinion, says zoologist Vicente Urios of the University of Alicante, who has followed the affair closely.

Jack Drenthe, AAP's representative in Spain, suggests that Cantó's change of heart is primarily inspired by a complaint filed by an Alicante businessman and developer who owns property adjacent to the site. But so far, the facility's backers have been unable to change Cantó's mind. Last month, famed U.K. primatologist Jane Goodall visited Relleu to show her support, but if anything, the visit "may have hardened the opposition," she says. A tumultuous town meeting on 30 July was dominated by the mayor and other opponents of the plan, says Urios, who chaired the event: "It's no longer a rational discussion."

Now, AAP is urging supporters to e-mail Cantó to show their support; it is also about to send letters signed by Goodall to members of the European Parliament and Spanish ambassadors across Europe. The Dutch government hasn't decided what to do if AAP misses its 2005 deadline, a spokesperson for the science and education ministry says.

Cantó could not be reached for comment, but Urios says he's unlikely to change his mind again. Luckily, he adds, other towns in the region are interested in providing the Dutch chimps with a tranquil, sunny old age. **–MARTIN ENSERINK**

ScienceScope

The Beagle Hasn't Landed

Blame it on the weather. A report released this week by the British consortium that built the ill-fated Beagle 2 Mars lander (*Science*, 28 May, p. 1226) speculates that the failure may have been due to unusually low pressure in the atmosphere during its descent to the planet's surface on Christmas Day of last year. Low pressure between 40 and 20 kilometers above the surface may have led the spacecraft to plummet too fast, resulting in a catastrophic crash on the martian sand and rocks, according to the 276-page study (ebulletin.le.ac.uk/news).

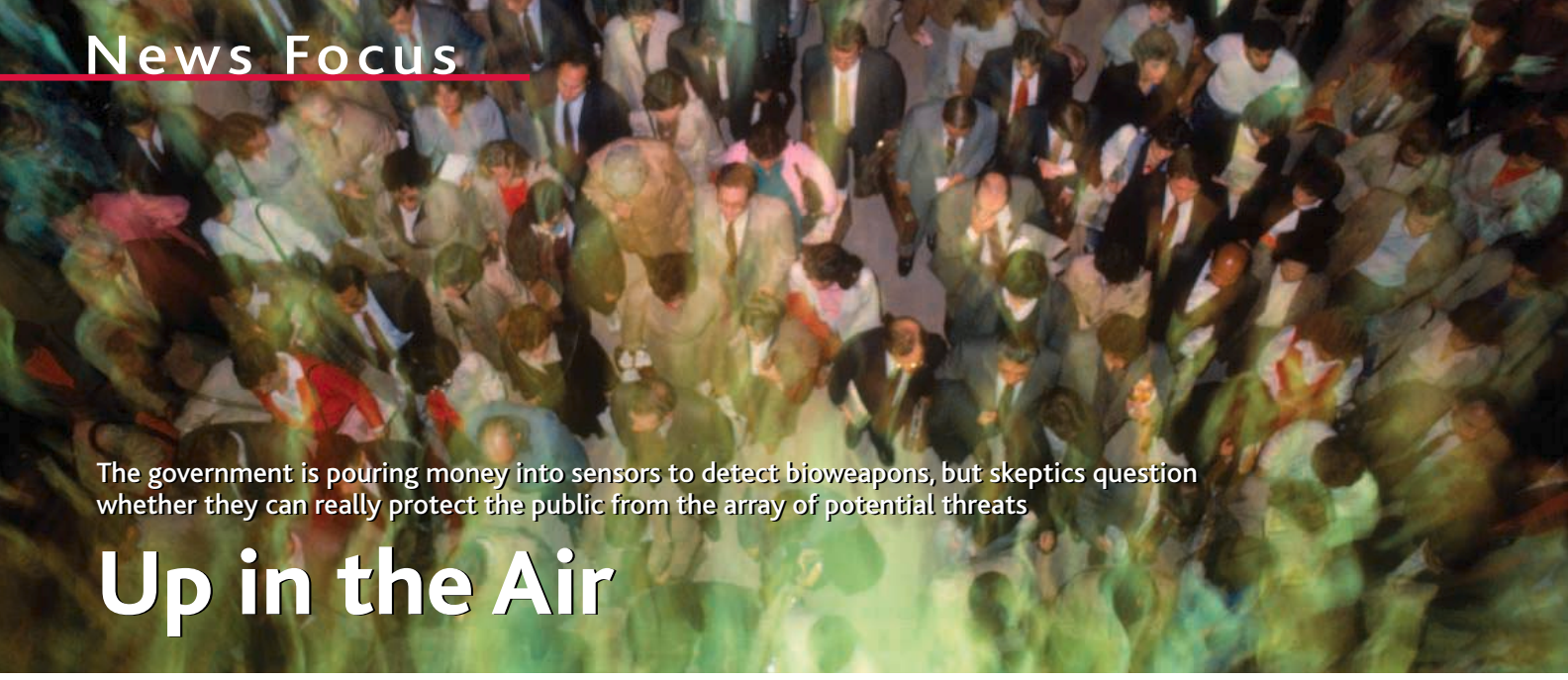
Other possible causes include electronics failure due to the intense cold of space, heat-shield breakup due to damage during testing on Earth, or problems with the parachute and air bags designed to smooth the landing. "A large number of failure modes are possible," states the study, but clear and compelling evidence for any single explanation is lacking. The report notes that a future lander should not be treated simply as an instrument and recommends that more time and resources be poured into better engineering and testing. The team concludes that it wants to "refly the payload as soon as possible" with a new and innovative design, but how and when remain up in the air.
–ANDREW LAWLER

Polio Campaign Suffers Setback

With new cases of polio reported for the first time in years in Mali and Guinea, and additional cases in Sudan's troubled Darfur region, the World Health Organization and African officials are acknowledging that they will not meet their goal of wiping out polio in 2004.

Last spring, the Global Polio Eradication Initiative in Geneva tried to erect a firewall of immunizations around Nigeria and Niger (*Science*, 2 July, p. 24). Mali and Guinea are outside that wall, "telling us that barrier needs to be much stronger and broader," says initiative chief Bruce Aylward. At the same time, within Nigeria, "we are still seeing the most intense transmission that we have seen anywhere in the world in years," he says.

The partners will now redouble immunization efforts in Mali, Guinea, and Chad as part of a synchronized campaign planned for 22 African countries in October and November. They still hope to knock out polio in the rest of Africa—and indeed the world—by year end. But with 476 cases to date in Nigeria, and at least 1000 expected by year end, Aylward concedes that they have to plan for continued transmission in Nigeria and Niger throughout 2005. **–LESLIE ROBERTS**



The government is pouring money into sensors to detect bioweapons, but skeptics question whether they can really protect the public from the array of potential threats

Up in the Air

Pentagon employees couldn't see the gas seeping into their building. They couldn't taste or smell it. But strategically placed sensors immediately picked up the problem, precisely tracking the wafting gas. Everyone was safe.

This was not reality. This was Pentagon Shield, a Department of Defense exercise last spring that simulated a biological or chemical attack. Research teams released sulfur hexafluoride—a harmless gas used in airflow testing—outside the Pentagon intermittently over several days. Standard gas analyzers traced its movement around and into the building, while other sensors recorded weather conditions. With those data, scientists are refining a computer model of aerosolized weapon movement.

In a real attack, however, unlike a neatly defined exercise, it's unclear how well actual sensors would perform. The Department of Homeland Security (DHS) spends more than $60 million annually on environmental detectors that monitor outdoor air for bioweapons, but many scientists argue that those detectors are ineffective. Now, DHS plans to spend at least $32 million more, over the next 18 months, to develop next-generation sensor technology.

"This research has tremendous promise," says Penrose Albright, assistant secretary for science and technology at DHS. But scientists remain skeptical that government contractors really can design sensors that quickly, cheaply, and accurately detect one of the dozens of bacteria, viruses, or toxins that could become aerosolized bioweapons (see table).

Hazardous history

Bioagents instill fear because just a little can pack a big punch. "Infectious biological agents are on the order of 1000 to 1 million times more hazardous than chemical [agents]," says Edward Stuebing, head of aerosol sciences at the U.S. Army Edgewood Chemical Biological Center in Edgewood, Maryland.

For decades, these worries were the quiet domain of U.S. military and national weapons labs, funded by the Department of Energy or the Defense Advanced Research Projects Agency. Researchers at Los Alamos National Laboratory (LANL) in New Mexico and Lawrence Livermore National Laboratory (LLNL) in California collaborated on an early biodetection network, dubbed BASIS. That eventually led to the sole environmental bioweapon sensor deployed nationwide today: BioWatch, an aerosol system that works like a vacuum cleaner, sucking air over filter paper that traps aerosol particles. Although earlier BASIS sensors were designed only to detect bioweapons during specific events, such as the Olympics, DHS has deployed BioWatch sensors to continually monitor air in more than 30 major cities.

Despite DHS claims of a perfect record, scientists privy to classified assays suggest that the sensors may experience false positives—mistaking normal environmental toxins for bioweapons. Others complain that because the assay results are classified, they have not been evaluated by outside scientists.

DHS's Albright characterizes BioWatch as a starting point, a relatively cheap system that can be upgraded with new technology. Much of the cost of BioWatch—roughly $60 million annually, or $2 million per city—is labor, he says: "Today, we collect the BioWatch filter, take it to the lab, treat the sample, do an initial screen, and then, if we get a hit, take it through an extensive battery of tests."

DHS wants a faster, sleeker system—one that continuously sniffs for bioweapons and can be sampled frequently with little maintenance, Albright says: "We want high sensitivity, minimal false alarms, and low cost, so we could deploy it nationally in large quantities and expect it to be maintained by, say, volunteer firefighters."

That's a big jump from today's BioWatch. But DHS's external funding arm, the Homeland Security Advanced Research Projects Agency (HSARPA), thinks it can make the leap. The agency recently launched its first research push, allocating more than $32 million to 14 outside teams.*

DHS is funding six teams to develop high-priority "detect-to-treat" systems. These would be deployed outdoors like BioWatch but would identify a bioweapon within just 3 hours, enabling doctors to treat exposed civilians. The remaining eight teams are doing feasibility studies for "detect-to-protect" systems, for use inside critical buildings and in specific outdoor spots, to detect a bioweapon within 2 minutes, in time to warn civilians and trigger responses in, say, ventilation systems.

"We are asking everybody to work as fast as they can," says Jane Alexander, deputy director of HSARPA. "In some cases, we have told bidders, 'We know we're asking for the sun, the moon, and four planets. If you can only give us two planets, go ahead." With DHS investment, several sensor prototypes probably could be deployed within months, says J. Patrick Fitch, head of chemical and biological national security at LLNL.

Fine-tuning

To build next-generation sensors, DHS hopes to tweak existing prototypes with the latest technology. Some sensors will run

* www.dhs.gov

CREDIT: TAXI/GETTY IMAGES

simultaneous assays on microchips, for instance, or tap new genomic markers for more definitive pathogen signatures.

All biosensors share two basic tasks: to sample air particles and to identify any pathogens. For sampling air particles 1 to 10 micrometers in size, a sensor includes one (or more) of several technologies. A vacuum, for instance, sucks air over filter paper to trap particles, as in the BioWatch sensor. Alternatively, a wetted cyclone draws air down a tube injected with water, which moves with centrifugal force to capture particles. A third variety, called a virtual impactor, uses tiny jets to push air particles down a tube at high speed, concentrating them while diverting excess air. Each differs in cost, sensitivity, speed, and complexity.

For the second task—isolating and identifying bacterial, viral, or toxic particles trapped in the sample—sensor systems typically run immunoassays, polymerase chain reactions (PCR), or mass spectrometry screens. Again, there are tradeoffs. Detect-to-protect technologies are relatively fast and cheap but often carry higher rates of false positives. "If I go from wanting an answer in an hour to wanting one in 2 minutes, I have eliminated all kinds of technologies, like PCR," says Fitch.

Although slower, the detect-to-treat sensors often use PCR to glean greater detail about a pathogen's identity, activity, and susceptibility to various treatment options. Among the DHS-funded teams, at least two detect-to-treat prototypes are already being field-tested. One is TIGER—for Triangulation Identification for Genetic Evaluation of Risk—developed by Science Applications International Corp. in San Diego, California, and Ibis, a division of Isis Pharmaceuticals in Carlsbad, California. TIGER works by sampling the air, extracting nucleic acids, and amplifying those acids with broad-based PCR primers that capture all biological agents in the sample. TIGER electrosprays the PCR products into a mass spectrometer that produces each agent's mass and DNA base composition. Scientists compare an organism's DNA signature with those in a broad database, confirming its identity—or, in the case of an unknown organism, using phylogenetics to characterize it. This process takes up to a day.

A similar sensor, the Autonomous Pathogen Detection System (APDS), has already been field-tested in the Washington, D.C., Metro transit system and at the San Francisco and Albuquerque airports. LLNL developed this sensor and licensed the technology to MicroFluidic Systems, which leads one of the DHS-funded research teams.

This sensor works by screening air particles with immunoassays or PCR analysis. By multiplexing—or running multiple tests simultaneously—an APDS unit can screen for more than 100 different bacteria or viruses in about an hour. Networked sensors communicate data to a remote console, often via wireless connection, so scientists get monitoring updates from afar. APDS can identify a known bioweapon in 30 minutes to 1.5 hours, Fitch says.

Faster detect-to-protect sensor prototypes are also emerging. One DHS-funded team leader, Johns Hopkins University's Applied Physics Laboratory (APL) in Laurel, Maryland, is developing a time-of-flight mass spectrometer that can, within minutes, identify a biological agent based on its proteins or peptides. APL's sensor automatically sucks in aerosol samples, mixes them with an ultraviolet light–absorbing chemical, and pulses the samples with UV light in a mass spectrometer. Based on light scattering and molecular weight, the system identifies key proteins, say, found in biotoxins. Such a system could instantly warn that bioagents may be present—and possibly trigger changes in ventilation systems or sound alarms. But the system offers less detail on pathogens than slower varieties do.

CDC Category Listing of Select Agents

CATEGORY A
- Anthrax
- Botulism
- Plague
- Smallpox
- Tularemia
- Viral hemorrhagic fevers

CATEGORY B
- Brucellosis
- Epsilon toxin of *Clostridium perfringens*
- Food safety threats (*Salmonella*, *E. coli*)
- Glanders
- Melioidosis
- Psittacosis
- Q fever
- Ricin toxin
- Staphylococcal enterotoxin B
- Typhus fever
- Viral encephalitis
- Water safety threats (*Vibrio cholerae*, *Cryptosporidium parvum*)

CATEGORY C
- Emerging infectious diseases such as Nipah virus and hantavirus

Close encounters. Researchers have begun field-testing biosensors in urban subway systems and airports, among other indoor venues.

CREDIT: TAXI/GETTY IMAGES

Wrong track

Still, skeptics question whether DHS's push for environmental detection is misguided. Microbiologist Paul Jackson of LANL argues that biosensor research is a costly diversion that will provide, at best, a false sense of security. "Everybody has aerosols on the brain," he says. "Frankly, I don't know that environmental monitoring of aerosols at random—or even in important places—is necessarily the best approach."

Jackson and others argue that more biodefense funds and government guidance should go to hospitals nationwide for "syndromic surveillance" or for the use of simple, reliable blood tests and other diagnostics to detect bioweapons. "The best sentries we have are patients who come into [emergency rooms] with suspicious symptoms," Jackson says. If an initial wave of bioterror victims was diagnosed quickly, he adds, many might be saved—and a nationwide alert could immediately be launched.

The federal government has already promised more than $2 billion in biodefense funds to local public health leaders, and the Centers for Disease Control and Prevention has urged those leaders to invest in syndromic surveillance. But local efforts are patchy—and, many say, poorly coordinated.

DHS also encourages syndromic surveillance. But its detection efforts begin in the environment, where questions first emerge. Did an attack actually happen? Can it be stopped? How can patients be treated? Can buildings be decontaminated?

Tradeoffs are likely to continue. Future bioterror weapons, scientists say, could include genetically engineered pathogens, prions, and bioregulators. All demand new sensors—and questions.

–KATHRYN BROWN

Loss of Dung Beetles Puts Ecosystems in Deep Doo-Doo

NEW YORK CITY—Some 1500 conservation biologists gathered at Columbia University from 30 July to 2 August to discuss humanity's growing impact on the natural world. Among the findings were new twists on how fragmenting forests can hurt dung beetles, monkeys, and other creatures.

Like an overengineered airplane, ecosystems are thought to have redundant functions that should prevent a single extinction from triggering more serious consequences. Many animal species disperse seeds, for example. So when one such species disappears, others face less competition and ought to become more abundant, taking up any slack.

Backlog. When key dung beetle species disappear, monkey dung goes unburied.

New research suggests that may not always be true. The study examined the fate of dung beetles, which collect dung, bury it, snack on it, and lay their eggs in it. Burying the seed-laden dung also enriches the soil and helps plants regenerate. Trond Larsen, a graduate student at Princeton University, found that the beetle species best at burying dung were the first to disappear from forest fragments. Alarmingly, related species did not become more abundant. Much dung then went unburied. "It tells us that the level of resilience in ecosystems to damage or biodiversity loss could be much less than we thought," says Richard Ostfeld of the Institute of Ecosystem Studies in Millbrook, New York.

Larsen studied 42 species of dung beetles in eastern Venezuela, where a hydroelectric dam completed in 1986 flooded 4300 square kilometers of tropical forest and created more than 100 forest islands. He found that smaller islands had fewer species of beetles and that the larger beetles were most frequently missing.

The main cause of the beetle's decline was a bad sense of direction. Most dung beetles are used to flying in contiguous forest, where they don't need to be expert navigators. By marking some 15,000 beetles and recapturing as many as possible, Larsen showed that beetles couldn't find their way back if they flew off the island. "Once they hit open water, they're done for," he says. Big beetles fly faster and farther than small beetles, he discovered, and are more likely to go AWOL. The problem is worse on smaller islands, where there is a larger perimeter relative to the area. To retain a viable population, three of the largest dung beetle species needed at least 85 hectares—a surprisingly large amount of habitat for an insect, Larsen says.

When beetle diversity declined, much less dung was buried. The remaining species of dung beetle on the smaller islands didn't become more abundant and dig into the surplus dung, Larsen found. The reason, he suspects, is that they too are accidentally leaving the islands, although at a lower rate. With fewer seeds being buried, forest diversity ultimately will decline.

The worrisome conclusion is that species diversity is less of a safeguard against ecosystem collapse than had been assumed, Larsen says: "Even the loss of just one or two species may have a much greater impact than we previously thought." Like top carnivores, the large dung beetles appear to be the most sensitive to extinction and extremely important for ecosystem integrity, he adds. Moreover, it's surprisingly hard for others to fill their shoes, Ostfeld says: "I wouldn't have expected to see this effect with a dung beetle."

Larsen's discovery that the beetle's larger body size and flying behavior make it more vulnerable to decline is an important contribution, says Ostfeld. "Finding a clear mechanism makes it more likely that ecologists can predict the systems that should behave similarly," Ostfeld says. "That's a big deal for environmental managers and policy specialists."

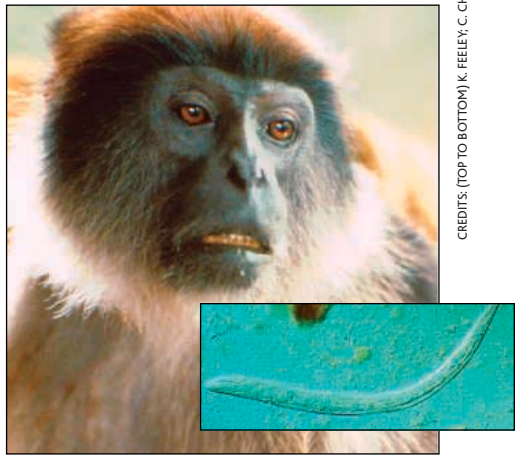
Forest Loss Makes Monkeys Sick

It's bad news for endangered animals when their habitats are fragmented. Populations become isolated, food supplies diminish, and hunters become more of a threat. Now add to that list a higher risk of illness.

Although it's known that disturbed habitat can help transmit diseases between wildlife and humans, a new study shows for the first time that fragmentation of forests by humans can hasten the decline of a primate population by making common parasites more abundant and introducing new ones. "It's a potentially devastating effect," says Peter Daszak, director of the Consortium for Conservation Medicine in Palisades, New York.

Deforestation threatens many populations of forest-dwelling primates in Africa. Thomas Gillespie, now a postdoc at the University of Illinois, Urbana-Champaign, and his Ph.D. adviser, Colin Chapman of the University of Florida, Gainesville, studied two species of leaf-eating monkeys to understand how habitat change might affect their health. They compared groups living in undisturbed forest within Kibale National Park in western Uganda with those living in surrounding forest fragments.

In the park, overall populations of both the Red Colobus monkey (*Piliocolobus tephro-*



CREDITS: (TOP TO BOTTOM) K. FEELEY; C. CHAPMAN; CDC

Homesick. Red Colobus monkeys that live in fragmented forests suffer from more parasites, such as *Strongyloides stercoralis* (*inset*).

sceles) and the Black-and-White Colobus (*Colobus guereza*) have remained stable. But in 22 nearby patches of forest, the scientists found that the total Red Colobus population fell by 20% between 1999 and 2003. In contrast, the number of Black-and-White Colobus in the same fragments rose by 4%.

Suspecting that parasites might be to blame for the decline in the Red Colobus, Gillespie and his team first looked for evidence of them in both fragmented and intact forest. Densities of primate parasites were higher in forest fragments, they found. For example, the larvae of the nodule worm *Oesophagostomum*, which causes the most debilitating symptoms of all the pathogens, were more than five times more abundant in the fragments. "It's very clear that there was a higher risk of infection in disturbed forest," says Gillespie. He suspects that people and livestock are introducing pathogens; indeed, four of the five parasites found only in the fragments also infect humans and livestock.

To measure the levels of infection, Gillespie examined 1151 monkey feces samples for parasites. Ten parasite species were present in the Red Colobus samples, and feces from fragmented habitat had significantly higher levels of most parasites than feces from the virgin forest. By contrast, the Black-and-White Colobus samples contained just seven parasites. For five of those parasites, there was essentially no difference in their prevalence between dung samples from fragmented and intact forest dwellers. That could help explain why the Black-and-White Colobus are doing better, although it's not clear why they would carry fewer parasites than do the Red Colobus.

"This work suggests a really strong role for disease" in the decline of the Red Colobus, says Nick Isaac, an evolutionary biologist at the Zoological Society of London. Although probably not fatal, parasites can affect a population indirectly, Isaac explains, by making monkeys less able to feed or conceive. And stress makes the animals more vulnerable to infection by parasites, which makes a grim situation even grimmer. **–ERIK STOKSTAD**

Profile John Schaefer

Shooting for the Stars

John Schaefer has driven Research Corporation to new heights in astronomy. But critics wonder if he'll ever relinquish the helm and whether something's been lost along the way

This fall, on a mountaintop in southeastern Arizona, astronomers from around the globe will celebrate first light at the world's most powerful optical telescope. They will also toast John Schaefer, the longtime head of Research Corporation (RC), the oldest scientific foundation in the United States. It was Schaefer who, in 1992, applied RC's weight—and eventually $12 million of its money—to pull what became the Large Binocular Telescope (LBT) from a mire of problems that was threatening to engulf it (*Science*, 22 June 1990, p. 1479).

Schaefer's rescue of the LBT was one of a series of bold moves that have changed the $150 million foundation since his arrival in 1982—not all of them successful, according to his critics. The LBT ceremony will also mark a rite of passage for Schaefer. The former organic chemist turns 70 next month and will step down at the end of the year as president and CEO of the atypical Tucson, Arizona–based charity. But he's not really leaving. Instead, he'll embark on what may be his most ambitious challenge yet: raising $200 million from both the public and private sectors to build yet another world-class observatory, the Large Synoptic Survey Telescope (LSST) (see sidebar). RC has committed $10 million to the venture as one of four founding partners and is providing office space for Schaefer and the LSST staff.

"He's very much a visionary, and he's been on the mark most of the time," says G. King Walters, a professor emeritus of physics at Rice University in Houston, Texas, and an RC board member since 1977. Patrick Osmer, a new board member and chair of the astronomy department at Ohio State University, which rejoined LBT in 1996, calls Schaefer "one of the smartest people I know and a remarkable leader."

But Schaefer's assertive leadership has also created a backlash. Two years ago, Schaefer suppressed what he viewed as a near-revolt within the organization by firing his designated successor, chemist Michael Doyle, and replacing four of the nine members of the foundation's board of directors. That insurrection was triggered by mounting concern over what Laurel Wilkening, a former chancellor of the University of California (UC), Irvine, and former board member, calls his "highhanded and autocratic" style of leadership. It's a style that has produced results, but his opponents say it is ill suited to a post-Enron era of greater corporate responsibility. "John's the kind of guy that you'd call in a crisis because he doesn't worry about consultation," says Wilkening. "He would take charge, and then tell us afterward what he had done. But times have changed, and he hasn't changed with the times."

The sky's the limit. RC's John Schaefer with the second 8.4-m mirror being polished for the Large Binocular Telescope.

CREDITS: RESEARCH CORPORATION

Research Corporation

Location: Tucson, Arizona

Founded: 1912

Current Endowment: $150 million

Focus: Research grants to faculty in the physical sciences at both predominantly undergraduate and Ph.D.-granting institutions; also invests in large projects and new scientific instruments.

A visionary in a hurry

Time is a relative term for Schaefer. "Right now I feel like I'm 25," he explained during an interview last month, surprised that anyone would question his decision to tackle a long-

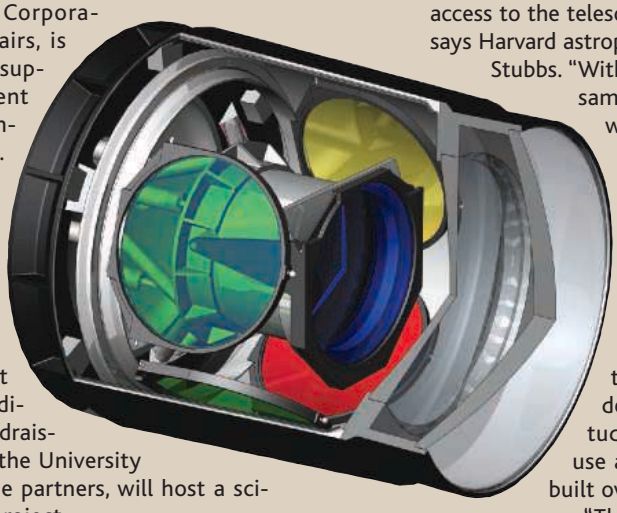
The Desire to Go Faint, Fast

Going "wide, fast, and deep" is the best way to explore the universe, according to astrophysicist J. Anthony (Tony) Tyson. For John Schaefer, it's another way for Research Corporation to make a difference.

The object of both men's desires is the Large Synoptic Survey Telescope (LSST), a $200 million instrument that would search for everything from the mysterious dark energy at the edges of the universe to asteroids that could threaten life on Earth. The three-mirrored optical telescope, sometimes called the Dark Matter Telescope, would peer much more rapidly and deeply into a wider swath of the heavens than any existing instrument. It would also deliver vast amounts of data to a global community of users.

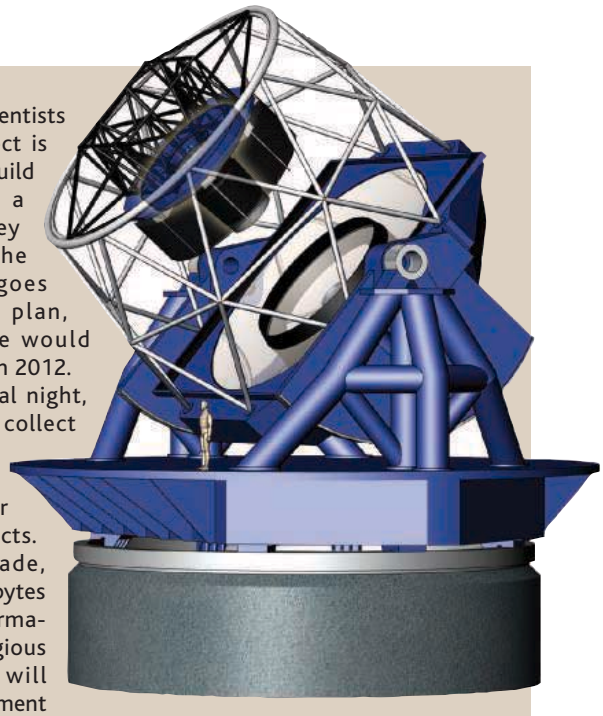
Schaefer, the outgoing president and CEO of Research Corporation (see main text), was seduced by the telescope's goal of addressing "one of the most fundamental questions of our time—will the universe collapse or fly apart?" It's the kind of bold venture that Schaefer says RC must pursue to remain relevant as a science charity. RC has already pledged $10 million, part of a $70 million pot that Schaefer has promised to raise from the private sector (lsst.org). In turn, Schaefer's vast network of contacts impressed Tyson, who had collected endorsements for a weak gravitational lensing telescope from three separate panels of the National Academies but nary a dime to design and build it.

The result is a partnership involving RC, the universities of Arizona and Washington, and the National Optical Astronomy Observatory. The LSST Corporation, which Schaefer chairs, is also seeking significant support from the Department of Energy and the National Science Foundation. "Everybody has their assignments," says Tyson, director of the project, who recently left Bell Labs for the University of California, Davis. "John's role is to know enough about the project to explain it [to] a lay audience and to lead the fundraising effort." Next month, the University of Washington, one of the partners, will host a scientific workshop on the project.



LSST's three mirrors—an 8.4-meter primary mirror, a 3.4-m secondary mirror, and a 5.2-m. tertiary mirror—will funnel light onto a 3.2-gigapixel camera in a design that creates a 10-square-degree field of view. That combination results in an optical throughput (the product of the telescope's light-collecting area and sky coverage, called etendue) of 300, some 60 times greater than those of existing telescopes such as the Sloan Digital Sky Survey. "The LSST will be the world's largest imager," Tyson says about the 1000-kg camera, capturing objects as faint as the 24th magnitude in 10 seconds and surveying the entire visible sky three times a month. "Wide, fast, and deep are not words that usually go together in astronomy."

Tyson says LSST will have an unprecedented ability to detect change, from swiftly moving near-Earth asteroids to dark matter as old as half the age of the universe. Schaefer says RC's initial contribution will allow the LSST Corporation to let a contract to design and construct the mirrors, showing other potential donors and scientists that the project is real. "If you build a mirror and a telescope, they will come," he quips. If all goes according to plan, the telescope would see first light in 2012.



All-seeing. The Large Synoptic Survey Telescope (*above*) will have a 3.2-gigapixel camera (*below*) at its heart.

On a typical night, the LSST will collect 30 terabytes of data on faint, rare, or transient objects. Over a decade, that's 30 petabytes of digital information—a prodigious output that will turn the instrument into a user-friendly facility. "The traditional model in astronomy relies on a committee that reviews requests for viewing time and controls access to the telescope, which can only do one project at a time," says Harvard astrophysicist and LSST system scientist Christopher Stubbs. "With the LSST, we can do multiple projects at the same time, and the data will be freely available, without any proprietary delays, to anyone who wants it—from the best scientists to a high school student doing a science project."

That approach will require huge advances in software and distribution technologies, however. And that's not the only obstacle facing Schaefer and Tyson. The LSST must also prove its mettle against another project, already under way, that is designed to tackle many of the same scientific challenges despite having an etendue one-fifth the magnitude of the LSST's. The $60 million project will use a handful of smaller, cheaper telescopes to be built over the next 5 years.

"The upside is that there are existing vendors who can build these smaller [1.4-m] telescopes quickly," says University of Hawaii, Honolulu, astrophysicist Nick Kaiser, PI for the Pan-STARRS project (pan-starrs.ifa.hawaii.edu). "The downside is that you need multiple detectors [cameras] and the software to connect them. But we think we can hold down the detector costs by applying our experience with similar detectors." The U.S. Air Force, which cares not at all about dark matter but a great deal about the technology for detecting threats to the planet, has already committed $20 million and is expected to foot the entire bill for construction.

Kaiser and his team hope to begin operating a prototype, atop Hawaii's Mount Haleakala, by early 2006. That gives Pan-STARRS quite a jump on the LSST, whose designs are still on the computer. "We think we've got a better approach, and Tony thinks he has a better approach," says Kaiser. "The community will decide whose approach—one massive instrument or many smaller ones—works better." **–J.D.M.**

CREDITS: RESEARCH CORPORATION

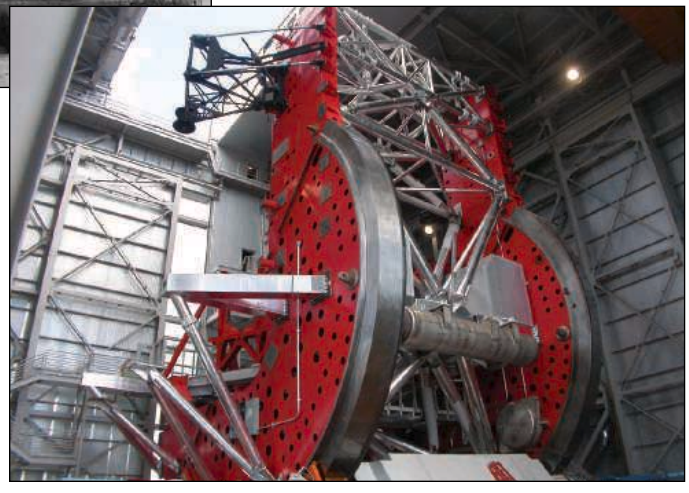
term project like the LSST when his peers are spending their days at the bridge table or on the golf course. Not that Schaefer has ever spent much time relaxing. His résumé includes becoming president of the University of Arizona in Tucson at the tender age of 36 and founding the university's acclaimed Center for Creative Photography, becoming sufficiently accomplished in the medium to coauthor a popular textbook with Ansel Adams. In 2002, when RC marked its 90th anniversary, Schaefer says he "took a couple of weeks" to pen a history of the foundation (www.rescorp.org).

By all accounts, Schaefer expects from others the same crisp efficiency that he demands from himself. "As department chair, I never met with John for more than 10 minutes," says University of Arizona astronomer Peter Strittmatter about his former boss—and current colleague on LBT's corporate board, which Schaefer chairs. "But I always left with an answer, even if it wasn't what I wanted to hear."

Schaefer's career is a classic immigrant's success story. The son of poor German parents who arrived just before the Great Depression lacking a formal education, he excelled in New York City public schools and worked as a carpenter to help pay his way through Brooklyn's Polytechnic Institute. In 1958, he received a Ph.D. in chemistry from the University of Illinois, Urbana-Champaign. Two years later Carl Marvel, a former president of the American Chemical Society and professor emeritus at Illinois, was headhunted by Arizona's Richard Harvill, who was trying to expand the school's regional reputation by recruiting world-class researchers. Marvel suggested that Schaefer join him in Tucson.

"I took to the city immediately," Schaefer recalls. And the university reciprocated, rocketing him through its ranks. In 1968, he was named department chair and in 1970 dean of the college of arts and sciences. Eighteen months later, he succeeded Harvill as president. Schaefer calls his promotions "a series of fortunate accidents." But he admits to a bit of ambition, too. "When Harvill announced his retirement, I thought, 'I'm liking this [dean's] job and enjoying having a greater degree of control over things. Why not go for the top job?' "

Schaefer took immediate advantage of his new authority to raise the university's research profile. He claimed control of all vacant faculty positions—typically the prerogative of individual departments—and held a campuswide competition to fill them. "It was a hunting license for department chairs to go after the best talent," he recalls. He also pooled overhead payments from federally sponsored research to create a discretionary fund that financed start-up packages and innovative research proposals. "We didn't use a committee because that isn't always the best way to make decisions," recalls Richard Kassander, an atmospheric scientist who was part of Schaefer's small, inner circle of senior administrators.



Telescope tradition. RC helped fund Grote Reber's work on his radio telescope, built in 1937 (*above*), and its support rescued the Large Binocular Telescope, nearing completion (*right*).

Old-timers say his most important step was getting Arizona (and its archrival, Arizona State) into an athletic conference that included prestigious schools such as Stanford and UC Berkeley. "Those relationships go beyond what happens on the athletic field," Schaefer says. "I wanted us to be associated in the public mind with top-notch schools." By all accounts, those efforts enabled his successor, Henry Koeffler, to make a successful bid to join the elite Association of American Universities, signaling the school's arrival as a major research institution.

Remaking RC

After 11 years at Arizona, Schaefer says he "had done what I wanted to do" and was ready for a change. It didn't help that the school's football team was facing a 2-year probation by the National Collegiate Athletic Association stemming from financial improprieties by its coach. "At my first press conference," says Koeffler, who took over in 1982, "every question was about athletics, not academics."

Meanwhile, RC was entering its eighth decade as an unsung, blue-chip charity and was looking for a new president with some pizzazz. Schaefer, who had joined the RC board in 1974, says that running a foundation "appealed to me." It also represented a golden opportunity to apply his management philosophy of "trying to make a difference" with whatever resources were available.

Research Corporation is not your typical foundation. It was founded in 1912 by Caltech chemist Frederick G. Cottrell as a way for the public to benefit from his invention of the electrostatic precipitator and other patents donated by university scientists. And it worked hard for its endowment: In its early years, RC operated as a business, making and selling precipitators; for decades it also helped commercialize university inventions, taking a share of the royalties. RC is best known for making small, early-career awards to promising physical scientists, including 30 Nobelists, using a process that Brian Andreen, a chemist who joined RC in 1964 and serves as its unofficial archivist, says was later copied by the National Science Foundation (NSF).

Schaefer's most dramatic move at RC was to create a separate nonprofit but tax-paying organization, Research Corporation Technologies (RCT), to handle RC's technology transfer activities. Schaefer says that the Internal Revenue Service had been warning RC for years that its dual functions of generating income from patent royalties and handing out grants could jeopardize its tax-exempt status. So Schaefer and a former Arizona colleague now at RC, Gary Munsinger, successfully lobbied Congress for a 1986 law that allowed RC to separate the two functions. Over the years, RCT has parlayed its initial $35 million "loan"—half of RC's endowment at

CREDITS: (TOP TO BOTTOM) NRAO; RESEARCH CORPORATION

the time—into some $300 million in working capital, with a current focus on seeding promising high-tech start-ups. In 1999, RCT even created its own scientific charity, the Frederick G. Cottrell Foundation.

Although Schaefer says RC had no choice but to divest its tech-transfer business, others aren't sure. Joan Valentine, a professor of chemistry at UC Los Angeles who this spring was ousted from the RC board, calls it "the biggest thing he did wrong. We were told there was no alternative, but I wonder." Walters, who also served on RCT's board, says he was "very disappointed that it came to pass." But he believes the RC board exercised "due diligence" in exploring its options.

Ousted. UCLA's Joan Valentine lost her board seat after criticizing Schaefer's management approach

Although RC and RCT are legally separate, Schaefer ran both organizations and chaired both corporate boards for several years. For good measure, he also headed the RC board's executive and nominating committees, giving him control over his corporate overseers as well as over the decision-making process. That's far too many hats for one person to wear, says Valentine.

A self-proclaimed political "naif," Valentine was part of a minority bloc on the board that had grown increasingly concerned about what it saw as Schaefer's "dictatorial" authority and the board's willingness to bend to his will. "The foundation, under its current president, is not interested in debate, dissent, or intellectual inquiry from those with different views," she wrote in an April 2003 memo to the board. "Given the demands and control of the president, this board has emasculated itself to the point of being irrelevant."

In particular, Valentine, Wilkening, and Robert Gavin Jr., a physical chemist and former president of Macalester College in St. Paul, Minnesota, who also resigned from the board in 2003, feared that RC was abandoning its historical mission. Instead of advancing the natural sciences through early-career awards and small grants that foster innovative research and teaching, RC was beginning to adopt what Wilkening called a "project-of-the-month" philosophy that relied upon Schaefer's particular preferences rather than rigorous scientific review. "I kept saying that we needed a long-range plan," says Gavin. "But all we got from John were ideas, one after another."

What went wrong

Three recent actions by Schaefer fueled those fears. The first was his bid in 2001 to run the U.S. government's preeminent network of ground-based optical telescopes, the National Optical Astronomy Observatories (NOAO). After turning around LBT, Schaefer thought the foundation was ready to become a national powerhouse in astronomy. But winning the contract would have imposed enormous strains on an operation tailored to making small academic grants, says Wilkening. "The proposal was put together in a hurry," says Wilkening, "and it always seemed like a stretch." In May 2002, NSF rejected RC's proposal and retained NOAO's longtime manager, Associated Universities for Research in Astronomy.

> "The foundation, under its current president, is not interested in debate, dissent, or intellectual inquiry. ..." —Joan Valentine

The second move was the abrupt dismissal of Doyle, Schaefer's handpicked successor. Doyle, who joined RC in 1997, had been named president in January 2002, although he continued to report to Schaefer rather than to the board. Six months later, however, Schaefer removed Doyle and reclaimed his old post. "It was a big blow and a shock to all of us," says Walters. "I have the greatest respect for Mike, and I did anticipate that Mike would succeed John."

Doyle accepted a financial settlement from the board and is now chair of the chemistry department at the University of Maryland. Neither he nor Schaefer will discuss the events that precipitated the separation, but some board members say the timing—following the loss of the astronomy proposal—is key. "I don't think that John ever cared very much about the grants programs; his passion was astronomy," says Valentine. "So the idea was that Mike would run the shop and John would take over all astronomy activities. Then NSF rejected our bid to run NOAO." With LBT going smoothly and LSST still only an idea, she speculates, "perhaps John felt RC was all he had."

The third controversy involves an environmentally friendly project to grow food along the Red Sea, to which RC made $4.6 million in loans in 2000. The Eritrea project, known variably as Seawater Farms and Seaphire, was the brainchild of Carl Hodges, then head of the University of Arizona's Environmental Research Lab. "The idea was to grow shrimp and use the effluent to grow halophytes [salt-loving plants]," Schaefer says. "And by not dumping the spent water back into the Red Sea, you could make it a closed system that would preserve the environment. It was a concept that the world needed," he says, and very much in line with having RC make a difference.

That's not how it looked to Valentine, who as head of the board's scientific advisory committee would normally have reviewed any project of this scale. "Carl's presentation was an embarrassment," she says. "It never actually came to a vote, however, because John decided to call it a special investment rather than a grant. That meant it could be handled by the finance committee," of which she was not a member.

Unfortunately, the investment was a bust. Current board members tend to blame political instability in the region, including the arrest of the government minister who supported the effort and a MiG attack by rebels on one of project's power plants. "Nobody on the board was a plant biologist or environmental scientist, but the pieces had been shown to work," says Stuart Crampton, a physicist at Williams College in Amherst, Massachusetts, and immediate past chair of RC's board of directors. Schaefer says that the project has been "mothballed" and that Hodges's recent request for support for a similar project in Mexico is a matter for his successor.

That would be biologist James Gentile, dean of the Natural Science Division of Hope College, an undergraduate institution in Holland, Michigan. Gentile, who says he expects to inherit Schaefer's titles as president and CEO when he takes the reins, acknowledges that Schaefer's tenure at RC will be a hard act to follow. Schaefer, he says, "casts a long shadow" on the foundation.

Valentine worries that it could turn into a dark cloud. "John is an irresistible force," she says. "So what will happen, for example, if the LSST comes up short? Will the board be pressured into giving more [than its $10 million pledge]?" More important, she says, "Will John let the new guy run the show?"

—JEFFREY MERVIS

CREDIT: PENNY JENNINGS

Sportfishers on the Hook for Dwindling U.S. Fish Stocks

New findings are likely to fuel debate over proposals to bar recreational anglers from some coastal waters

Call it the mystery of the disappearing fish.

Despite decades of tighter restrictions on commercial fishing, the populations of many U.S. fish stocks have continued to decline. The puzzle intrigued marine ecologist Felicia Coleman of Florida State University in Tallahassee nearly a decade ago, when she served on a government panel that helps set regional catch limits. Coleman noticed that recreational fishers were hunting many of the at-risk species the council was trying to protect. While commercial fishers were on the regulatory hook, were sport anglers the ones that got away?

The notion that hobby anglers pose a major threat to marine fish is controversial. Many U.S. sportfishing groups, for instance, have opposed restrictions on their pastime by claiming just 2% of the overall fish landings—despite estimates that 50 million Americans participate in the sport. These low-catch claims have been politically persuasive, says Andrew Rosenberg, a marine biologist at the University of New Hampshire in Durham and a former deputy director of the National Marine Fisheries Service. "It's hard to convince people that one guy on a boat could be causing a problem," he says.

That may be about to change, however, thanks to Coleman. In an extensive analysis of fisheries data published online this week by *Science* (www.sciencemag.org/cgi/content/abstract/1100397), her research team concludes that sportfishers are having a much bigger impact on marine populations than had been thought—and that they represent the major human threat for some species. Sportfishers are responsible for the vast majority of the landings of some at-risk species, according to the study, and have landed about 5% of the average annual catch over the last 2 decades.

Such numbers highlight the need for new restrictions on sportfishing, say marine conservationists, including barring anglers from new "no-take" reserves in coastal waters. Sportfishing groups, however, say the statistics don't necessarily support that solution. "You don't need to stop people from enjoying the outdoors" to protect fish, says Michael Nussman, president of the American Sportfishing Association (ASA) in Alexandria, Virginia.

To obtain the new numbers, Coleman's group cast a wide net, collecting 22 years' worth of landings data from state and federal agencies. Overall, they found that recreational landings accounted for 4% of the 4 million metric tons of marine finfish brought back from U.S. waters in 2002 (the most recent year for which statistics are available). But sport anglers had a much bigger impact on some species and in some regions. When the researchers focused on several dozen overfished species such as red snapper and red drum, they found that one-quarter were being landed by recreational fishers. Sport anglers take one-third of the catch of at-risk species in the South Atlantic and two-thirds of those in the Gulf of Mexico.

Drumming up controversy. Sport anglers may be a major threat to some overfished species, such as this red drum.

The study also questions another bit of conventional wisdom—that sport fishers do less harm to marine ecosystems than commercial fleets. Not so, report the researchers, because they often hunt top predators, causing ripple effects throughout the ecosystem. "It doesn't matter whose hook is in the water," Coleman says.

"This is by far the best assembly of landings data" to date, says Ray Hilborn, a fisheries scientist at the University of Washington, Seattle. He says it shows that "the recreational fishing industry is a much bigger problem than it would like to think it is." Rosenberg predicts that the findings will have political ramifications by bolstering opposition to "freedom to fish" bills that have been introduced in Congress (S. 2244 and H. 2890) and in a dozen coastal states. The bills seek to counter growing efforts to establish no-fishing zones by forcing government officials to show that alternative approaches won't help threatened species.

Recreational fishers, meanwhile, note that the landings data underpinning the study can be notoriously unreliable. And even if the numbers are accurate, they argue that no-take zones should be a last resort. "We have a good track record of conservation," says ASA's Nussman, noting that traditional restrictions—such as catch limits and seasonal closures—have helped restore some threatened populations, such as striped bass along the Atlantic coast. "We'll do what we need to do to fix the problem."

Marine researchers, however, aren't convinced that traditional approaches will be enough to protect dwindling stocks. Even bag limits, Coleman notes, only restrict the number of fish that can be caught by an individual fisher, not the total number caught by all sport anglers. "Right now, it's open access for recreational fishers," she says. "We need to fix that."

Commercial fishers, meanwhile, are happy to be out of the spotlight. Studies like Coleman's support what commercial captains have been saying for years, says Robert Jones, executive director of the Southeastern Fisheries Association in Tallahassee, Florida: "We're not the only ones causing the problem." Still, Jones is skeptical that the new data will produce policy change. "The recreational fishing industry has very strong political connections," he says.

The strength of those connections will be tested early next year. That's when several state legislatures are expected to consider freedom-to-fish proposals. The next Congress also plans to resume work on a major overhaul of federal fisheries regulation.

–DAVID GRIMM

CREDIT: BUDDY MAYS/CORBIS

RANDOM SAMPLES

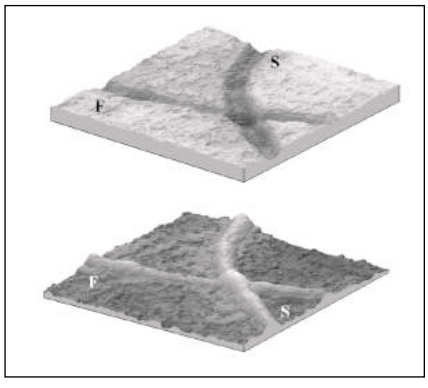
Edited by Constance Holden

Handwriting Analysis Goes 3D

A new technique that uses three-dimensional holograms to analyze handwriting samples may expose writing characteristics that forgers can't fake.

Traditionally, forensic handwriting experts try to spot forgeries by analyzing the pen strokes used to create a signature. But it's difficult to discern these "stroke dynamics," especially in the work of a skilled forger.

So scientists at the Università degli Studi "Roma Tre" in Rome are using a hologram generator to make 3D reconstructions, transforming handwriting into landscapes of hills and trenches that reveal the pressure and stroke sequence used to create each letter. For example, when strokes made with a ballpoint pen cross each other, the second stroke clearly cuts across the first if it's made with equal pressure. These are details that "you wouldn't be able to see on a microscope," says co-author Lorenzo Cozzella, an electrical engineer. Tests of various combinations of pen and paper types in 126 different signatures revealed that the holographic image indicated the proper stroke order in almost 90% of cases, the authors report in the 10 August *Journal of Optics A*.



Ballpoint pen marks on paper (top) and reversed image (bottom) showing bump where lines cross.

Charles Berger, a document examiner at the Netherlands Forensic Institute in The Hague, is skeptical of the researchers' claims, which, he says, "will have to be supported by experiments in which factors such as the writing pressure and paper support are controlled." But "if it really works, it would be a valuable tool for forensics," says Venu Govindaraju, a pattern recognition expert at the University at Buffalo in New York, who notes that the problem of forgeries is "rampant."

Rare Albino Elephant

Wildlife biologists in Sri Lanka last month took unprecedented photos of a white elephant (center) in the wild. A female about 11 years old, she was spotted in a herd of about 17 elephants. Dayananda Kariyawasam, director of Sri Lanka's Department of Wildlife Conservation, said scientists intend to collect dung samples to see if they can determine the genetic mutation for albinism, which is extremely rare in elephants.

Obesity Watch

The United States' "epidemic" of obesity and couch-potatohood continues unabated, according to two recent reports.

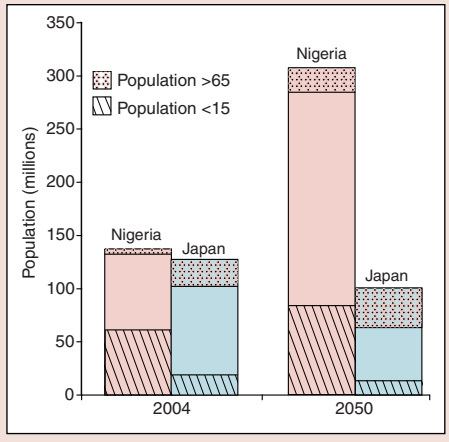
A federal interagency report on *America's Children* released last month relates that 15% of children between 6 and 18 were overweight as of 2000. Mexican-American boys now lead the pack: 30% of Chicano adolescents were overweight by 2000. Next highest risk are black girls, 24% of whom are overweight.

Prospects for a slimmer future are not great, judging by another study, published last month in the *American Journal of Preventive Medicine*. A team of scientists at the University of California, Los Angeles, headed by Antoinette K. Yancey, found from a telephone survey of 8353 L.A. adults that 41% acknowledged "sedentary" existences. Sedentary was defined as "no continuous physical activity for at least 10 minutes weekly at any level."

Time for state intervention? "The U.S. epidemic of obesity and sedentariness is now of sufficient societal magnitude and cost that increasing physical activity participation can no longer be treated as solely an individual responsibility," the authors intone.

Two Different Worlds

The demographic divide that cleaves the world, largely along north-south lines, is getting ever more pronounced, the Population Reference Bureau (PRB), based in Washington, D.C., noted last week in its annual data report. Although population in the developed world has pretty much leveled off—and is actually declining in countries other than the United States—the rest of the world continues its precipitous climb despite high infant mortality in some areas, such as Africa.



The PRB exemplified the trends in a comparison of Nigeria and Japan, countries of similar population size but with very different population trajectories.

CREDITS: (TOP TO BOTTOM) PRITHIVIRAJ FERNANDO; SPAGNOLO *ET AL.*; SOURCE: PRB

PEOPLE

Edited by Yudhijit Bhattacharjee

CAMPAIGNS

Mobilizing millions. Lee Iacocca, the former auto executive who created the Ford Mustang, is asking 1 million Americans to donate $10 each to fund a clinical trial of a novel diabetes treatment. Scientists at Massachusetts General Hospital in Boston have struck out finding money from conventional sources.

Mass General immunobiologist Denise Faustman reported in *Science* last year (14 November 2003, p. 1223) that injecting adult spleen cells into diabetic mice allowed their pancreases to regenerate, offering a potential treatment for type I diabetes. The Food and Drug Administration gave Mass General the go-ahead to try to replicate the approach in humans using an already-approved drug, but funding sources such as the Juvenile Diabetes Research Foundation were unconvinced that it was a bigger priority than other experimental treatments.

That's when Iacocca, whose wife Mary died of type I diabetes more than 20 years ago, stepped in. He says he wrote a personal check to Faustman for $1 million before asking the public to help. "We have not had any success getting support from other groups," says Iacocca, and "I decided I didn't want to wait." He hopes to raise enough money by the end of the year.

IN MEMORIAM

Canadian tragedy. The University of Toronto is setting up a scholarship to honor an engineering student killed while driving a solar-powered car he helped build for a school project.

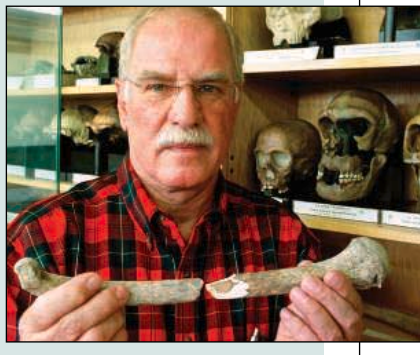
Andrew Frow, 21, died 12 August while participating in the inaugural 10,000-kilometer Canadian Solar Tour across Ontario and Quebec. Frow lost control of Faust II and veered into the path of an oncoming minivan shortly after the six-car convoy started out from Windsor, Ontario. Police speculate that gusting winds may have caused the 190-kg car to fishtail out of its lane. Officials immediately canceled the tour.

Frow's family says Andrew "was passionate about the project," and they hope solar-car enthusiasts will continue developing the technology.

ON CAMPUS

Alleged skullduggery. A German anthropologist who's been accused by his university of peddling chimpanzee skulls that don't belong to him is now facing questions about his research, too.

Reiner Protsch von Zieten, the former director of the Institute of Anthropology and Human Genetics for Biology at Goethe University in Frankfurt am Main, Germany, was put on leave by the university in April after officials said he had tried to sell 280 chimpanzee skulls for $70,000. The university says the skulls belong to its collection; Protsch has told reporters that he bought them from a Heidelberg doctor nearly 30 years ago.



Last week, the weekly magazine *Der Spiegel* added to Protsch's woes with a report that several fossils originally dated by Protsch have been found to be several thousand years younger than he had claimed. According to the magazine, the fossils were reexamined as part of a larger study of Paleolithic fossils by archaeologists Thomas Terberger of the University of Greifswald and Martin Street of the Research Center for the Early Stone Age in Neuwied. Protsch told *Der Spiegel* that the new measurements are wrong.

Although the misconduct accusations are serious, says anthropologist Carsten Niemitz of the Free University in Berlin, the impact on the field is "marginal" because of ongoing work that will answer questions about who was living in Germany 30,000 years ago.

POLITICS

Tit for tat. Michael Reagan, son of the former president and his first wife Jane Wyman, will defend President George W. Bush's stem cell research policies at the Republican national convention next week in New York City.

Brother Ron, a Democrat, made a plea for expanded stem cell research at the Democratic convention last month (*Science*, 23 July, p. 473). News reports indicate that the Republicans lined up 59-year-old Michael after it became clear that Nancy Reagan would not be attending the convention.

Michael, who lives in Los Angeles, is host of a conservative talk show that airs on the Internet and on satellite radio. On a recent broadcast, he observed that not all the Reagans endorse human embryonic stem cell research, saying, "my father, as I do, opposed the creation of human embryos for the sole purpose of using their stem cells as possible medical cures."

DEATHS

Nobelist. Sune Bergstrom, the biochemist who shared the 1982 Nobel Prize in physiology or medicine for his work on prostaglandins, died in his native Sweden on 15 August. He was 88.

Cloning researcher. John Clark, the head of the Roslin Institute in Edinburgh, U.K., was found dead in his vacation home along the Berwickshire coast in Scotland on 12 August. The 53-year-old Clark played a role in the creation of Dolly and became Roslin's director in 2002.

Got any tips for this page? E-mail people@aaas.org

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LETTERS

Finding Evidence for Black Holes

I READ G. C. BOWER *ET AL.*'S RESEARCH Article "Detection of the intrinsic size of Sagittarius A* through closure amplitude imaging" (30 Apr., p. 704; published online 1 Apr.; 10.1126/science.1094023) with alarm. Like many before them, the authors are presuming too much about black holes, considering the present state of knowledge. Black holes are popular topics of conversation, beloved of science fiction writers, but, as yet, not one has been identified beyond all reasonable doubt. Indeed, although there is strong evidence for the existence of black holes, it is not compelling because there is no proof yet that any of the candidates possesses that defining property of a black hole, an event horizon.

Various claims have been made for black hole candidates (*1*, *2*), but none stand up to one simple test. From general relativity, it follows that for a black hole, the ratio of mass to radius of the event horizon must satisfy $M/R \geq 6.7 \times 10^{26}$ kg/m.

In neither of these cases is this inequality satisfied or the existence of an event horizon even considered. Again, in the case of Bower *et al.*, the data provided do not lead to this inequality being satisfied. Interestingly, this quoted relation is precisely the expression for the ratio of mass to radius that Michell derived in 1784 (*3*) for a body possessing an escape speed greater than, or equal to, that of light.

A possible alternative explanation for the above observations could be the presence of quark or even subquark stars (*4*, *5*) clustered near the center of our galaxy. Such an explanation gains some credence from simple order of magnitude calculations. Alternatively, the central mass could be composed of a mixture of baryonic and dark matter that could involve a number of normal stars of roughly solar mass, contained within a distributed source of gravitation able to constrain the mixture within a stable limited volume forming the galactic center. It is too early to rule out completely other explanations for relatively recent observations. If black holes do exist and there is one at the center of our galaxy, care must be taken not to claim proof of its existence until its presence is established beyond all reasonable doubt. That point has not been reached yet.

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Response

DUNNING-DAVIES'S ALARM IS MISPLACED. WE have certainly not claimed proof of the existence of black holes on the basis of our research. In fact, our research is motivated in part by the desire to find the strongest possible evidence of the existence of black holes. We are well aware that current efforts fall short of excluding all possible alternatives to the black hole hypothesis for Sagittarius A*. Demonstration of the black hole mass-radius relation would be compelling evidence, for instance. Our recent limit on the size of the radio-emitting region of Sgr A* combined with astrometric measurements showing that Sgr A* is virtually motionless with respect to the Galaxy (*1*) provide the tightest constraint yet on the mass density of a black hole system. Yet this limit is about five orders of magnitude less than the canonical black hole mass density. Future imaging and astrometric experiments will narrow this gap substantially in the coming decades. Nevertheless, the current density limit is sufficient to eliminate all existing alternative models on the grounds that clusters of particles or compact objects such as strange stars would evaporate on time scales much, much less than the age of the Galaxy (*2*).

Evidence for or against black holes, of course, can be obtained on the basis of studying the numerous other properties determined by the space-time metric in their vicinity (*3*). Ultimately, we hope to achieve a resolution of only a few Schwarzschild radii through submillimeter very long baseline interferometry. With such an experiment, we expect to see the effects of the black hole's mass and spin on radiation emitted at small radii (*4*).

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Extending Life-Span in *C. elegans*

THE LIFE-SPAN OF THE NEMATODE *CAENORHABDITIS ELEGANS* can be extended by at least six different mechanisms, including calorie restriction, reduced Ins/IGF-1 signaling, germline ablation, food sensing amphid ablation, mitochondrial deficiency, and decreased temperature. Reduced Ins/IGF-1 signaling and calorie restriction can also increase the life-span of flies and mice. The Brevia "Healthy animals with extreme longevity" by N. Arantes-Oliveira *et al.* (24 Oct. 2003, p. 611) showed that *daf-2* RNAi treatment and gonad ablation of worms carrying the *daf-2(e1368)* hypomorphic mutation in the gene encoding the *C. elegans* Ins/IGF-1 receptor increases their life-span 6.0-fold. We have found that the average life-span of *daf-2(e1370)* mutants grown in axenic medium [a sterile liquid medium based on yeast extract, soy peptone, and hemoglobin; see (*1*)] was 90.9 days, representing a 6.3-fold life extension and a 7.5-fold adult life-span extension relative to wild-type controls grown on plate cultures seeded with live *E. coli* cells (*1*).

Arantes-Oliveira *et al.* also note the health of their long-lived worms. We observed that worms grown in axenic medium appear more vigorous than their monoxenically grown counterparts and that these worms exhibit an increase in metabolic rate (*2*), counter to the idea that a reduction of the metabolic rate is associated with a longer life-span. Moreover, both caloric restriction and reduced Ins/IGF-1 signaling increase the resistance to heat and oxidative stressors (*1*), and calorically restricted mice are less prone to age-related diseases. Thus, the life of worms can be extended without diminishing health. These results might be important for human aging as well, because both caloric restriction and cell signaling have been shown to regulate the aging rate in organisms ranging from yeast to mammals.

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Disagreements Over Cloud Absorption

IN THEIR LETTER "HAVE CLOUDS DARKENED since 1995?" (14 Nov. 2003, p. 1151), Z. Li and colleagues discuss points raised in an earlier news article on climate models and clouds ("Making clouds darker sharpens cloudy climate models," R. A. Kerr, News of the Week, 20 June 2003, p. 1859). Li *et al.* state that "Agreements [between model calculations and observations] within the range of uncertainties were found by all teams… except for one…," where a paper of ours is cited (*1*) as the exception and no references are given for "all teams." This statement is misleading and inaccurate. Cloud absorptances were calculated in (*1*) with a suite of five different radiative transfer models, and, contrary to Li *et al.*'s Letter, agreement within the uncertainties was indeed found for most models. Figures 11 and 14 and Table 3 in (*1*) show observed and modeled absorptances and the overlap of error bars. For example, in the 29 March case [the most favorable case for measurements and analysis (*2*)], the differences are 20 to 23 W m^{-2} for three models and 61 W m^{-2} for the two other models (*1*). Other ARESE II studies find measurement-calculation differences of 18 to 35 W m^{-2} (*3*) and 15 to 28 W m^{-2} (*4*). Hence, the results in (*1*), (*3*), and (*4*) are in general agreement (given model and measurement errors and variations in model implementation between the various studies) for the higher performance models. Very importantly, however, all the studies find systematic model-observation discrepancies.

In our view, the true disagreement in the few cases studied is on the interpretation of the model-measurement differences. Li *et al.* and Ackerman *et al.* (*4*) appear to conclude that cloud absorptance can be calculated adequately, whereas Valero *et al.* (*1*) and O'Hirok and Gautier (*3*) conclude that model-measurement differences, even if within error bars, are important because of their systematic character; models consistently underpredict and never overpredict the value. The source (experimental or modeling) of such a bias is of major concern because these results are fundamental for both climate and remote sensing applications.

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Response

THE PURPOSE OF OUR LETTER WAS TO REFUTE a misimpression left by a news article by Richard A. Kerr: that atmospheric radiation models have become a lot more absorbing as a result of the claim of enhanced cloud absorption in 1995. In fact, the best models are not much more absorbing now than in 1995, and their extra absorption is due to gases and aerosols and a better treatment of surface albedo, not clouds. What is true about models is that many climate-model radiation packages were too transparent (*1*); this was brought to the community's attention by a few studies comparing modeled and observed solar energy disposition (*2–4*) that were published in 1995, independently of the enhanced cloud absorption controversy.

Our discussion of Valero's work was a side issue not directly related to this main point about whether models have really changed radically or not and the main factors driving the changes. The conclusion of his study seems to be rather mixed. If we misinterpreted his results, we apologize. We are not denying that there may still be a bias between models and measurements, nor are we denying the reality of disagreements that existed in 1990 as summarized by (*5*). We are merely saying that the general increases in atmospheric absorption in Global Climate Models since 1995 have been attributed much more to the treatment of clear-sky solar radiative transfer processes than to the cloud absorption. In spite of the substantial progress in observational technology since 1995, spurred by the controversy, we are still not at the point where the bias can be unambiguously separated from possible measurement error. More field campaigns with even better technology are necessary to nail down the remaining much smaller bias.

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CORRECTIONS AND CLARIFICATIONS

News of the Week: "Lab fails to reproduce protein's appetite-suppressing effects" by T. Gura (9 July, p. 158). The article stated that "leptin failed as a drug." Amgen of Thousand Oaks, California, which has an exclusive license from Rockefeller University to develop leptin, reports that it has discontinued commercial studies of leptin for obesity, but is supporting research on its possible use in therapy for general lipodystrophy.

News of the Week: "Report accuses Bush Administration, again, of 'politicizing' science" by A. Lawler and J. Kaiser (16 July, p. 323). The article incorrectly characterized a statement by Janet Rowley regarding her White House interview before being appointed to the President's Council on Bioethics. Rowley did not contact the council chair, Leon Kass, after being questioned about her support for President Bush and his policies.

Reports: "Role of NMDA receptor subtypes in governing the direction of hippocampal synaptic plasticity" by L. Liu *et al.* (14 May, p. 1021). The legend for Fig. 1C, which reads "HFS failed to produce LTP in the presence of NR2B antagonists," is incorrect. It should read "NR2B antagonists failed to block HFS-induced LTP."

PHILOSOPHY OF SCIENCE

A Call for a Collective

Naomi Oreskes

Over the past twenty years, the dominant trend in science studies has been to emphasize the social dimensions of science: that research is performed in socially organized settings, that individual initiative and curiosity are focused and mediated by the concerns of the sponsors and consumers of scientific work, and that scientific claims are established as scientific knowledge through socially constituted processes of negotiation and consensus. This has been a useful corrective to earlier work in philosophy of science, which had produced a falsely individualistic and idealized view of scientific practices and the establishment of scientific knowledge. The difficulty with this corrective, like so many others, is that it often goes too far. There has been a tendency among some authors to imply that the social dimensions are what really matters (because all the rest is window dressing), the results of scientific work nothing but social constructions. Such a view is clearly as wrong as the one it replaces, as it fails to account for the efficacy and influence of the natural sciences in comparison to other human activities. (After all, those engaged in these other activities have access to all the same social resources as do scientists). Worse, it has led to silly and sterile arguments about whether there is or is not a real world and whether scientific knowledge bears any relation to it (if it exists). Of course there is a real world, and of course scientific knowledge bears some relationship to it; the question is what sort of relationship, and what can we do with it?

This is the question posed by Bruno Latour. In *Politics of Nature*: *How to Bring the Sciences into Democracy*, he picks up an argument begun in his earlier work, *We Have Never Been Modern* (*2*), that the dichotomy between nature and society—between the world and our representations of it—is false. Furthermore, Latour argues, there is no separation between science and nature, for nature is itself a concept that results from certain kinds of scientific and social framings, and so, for that matter, are science and society. These concepts are interdependent and intertwined, and they must be understood collectively. There is a real world, but it is not "out there." Latour's goal is to apply this insight to the question of political ecology, which he defines as "the understanding of ecological crises that no longer uses nature to account for the tasks to be accomplished. It serves as an umbrella term to designate what succeeds modernism according to the alternative 'modernize or ecologize.'"

Politics of Nature
How to Bring the Sciences into Democracy
by Bruno Latour

Harvard University Press, Cambridge, MA, 2004. 319 pp. $55, £35.95, €50.70. ISBN 0-674-01289-5. Paper, $24.95, £16.95, €23.10. ISBN 0-674-01347-6. Translated by Catherine Porter (*1*).

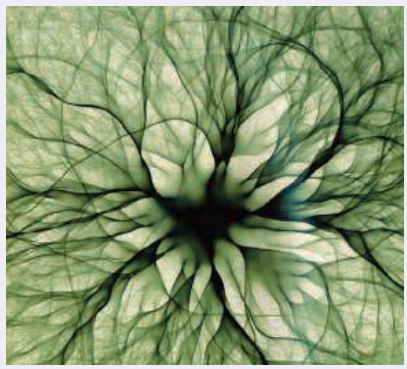
As this definition might suggest, Latour's writing is complex and idiosyncratic. Despite his considerable efforts to make his argument clear (including chapter synopses and a glossary at the end), it would be difficult to say that he entirely succeeds. The book runs from a variety of directions at the same basic theme, which seems to be this: nature has been viewed as one and cultures as many, with a sharp divide presumed between nature and cultures. In reality, natures are as many as cultures, because we define nature, and there are many human-nature possibilities.

Latour's particular focus here is ecology, and he suggests that to address ecological damage and destruction, we have to first acknowledge and then reject the false separations we have heretofore accepted. We have to reject the idea that nature is incontestable, apart and independent from politics and culture. "[U]nder the pretext of protecting nature, the ecology movements have also retained the conception of nature that makes their political struggle hopeless. Because 'nature' is made…precisely to eviscerate politics, one cannot claim to retain it even while tossing it into the public debate." His proposal is to replace this bifurcated world with a collective based on civil collaboration between humans and nonhumans, using "an ever growing list of associations between human and nonhuman actors." Thus his argument is simultaneously about science and about political discourse and institutions.

First, some complaints. While Latour frequently insists on his respect, even admiration, for scientists, the language he chooses often seems to imply nefarious intent. His use of the term fabrication, for example, to describe the complex process of stabilizing scientific facts, could be viewed as innocent (fabrication equals making) or not (fabrication equals fraud). Or consider his definition of "Science" as "the politicization of the sciences through epistemology in order to render ordinary political life impotent through the threat of an incontestable nature." Scientists will take offense at the conspiratorial implications of such a definition (that is, if they understand it); historians will doubt that people are that organized.

Latour also credits science with being far more powerful than it nowadays seems to be. Climate scientists have argued at considerable length that global warming is a fact—part of incontestable nature—but this has not stopped politicians, economists, business executives, and others from contesting it. Indeed, scientists' power to determine the "incontestable" facts of nature is itself highly variable—sometimes it works, sometimes it does not. Latour's analysis leaves us at a loss to understand why this should be the case.

Nevertheless, Latour has a point: by claiming that something is natural, we strongly imply that we must accept it, like it



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BROWSINGS

Super Vision. A New View of Nature. *Ivan Amato*. Abrams, New York, 2003. 232 pp. $40, C$65, £25. ISBN 0-8109-4545-2.

Scientific instruments often capture beauty as well as data. The striking and informative images in this collection depict phenomena across 42 orders of magnitude of spatial scales, from the collisions of subatomic particles to the microwave anisotropy of the universe. Amato accompanies his descriptions of what is being shown with explanations of the underlying technology. (Above, a computer simulation, by Eric Heller, of electrons flowing in a semiconductor.)

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or not. Conversely, by defining something as unnatural, we label it rejectable. (Hence the enormous arguments over the biological origins of homosexuality.) By artificially separating nature from culture, we close off discussion. All things "natural" are excluded from political analysis. Truly, we should know better. After all, not so long ago, we rejected miscegenation as unnatural; today we reject that rejection as racism.

Moreover, Latour raises at least one point that strikes this reader as exactly right: that to make ecological discussions meaningful, nonhumans have to be considered equally with humans. We must extend Kant's categorical imperative—to treat humans as ends, rather than means—to the nonhuman world as well. This means taking seriously the interests, needs, and even desires of nonhumans. Although this might seem daft at first—how can we know the desires of trees?—Latour points out that scientists routinely speak about non-humans (for example, neutrinos, viruses, crustal plates, frogs), often as if speaking for them. Who hasn't heard scientists talk about the crust wanting to move, viruses needing to replicate, and trees striving to reach the forest canopy? So it is not so great a stretch to consciously consider the interests of plants and animals, of the oceans and atmosphere, as well as (not incidentally) the interests of future generations of humans. Indeed, this may well be the only way to counter the ubiquitous tendency of currently living humans to act as if only they existed, or in any case as if only they mattered.

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NOTA BENE: OCEANS

A Decktop View of Overfishing

Moored alongside the piles of discounted titles in British bookstores this summer is Redmond O'Hanlon's log of two weeks spent on a Scottish trawler. O'Hanlon is best known for his stories of careering journeys around various tropical forests, his aim being to understand the psychology of travel under extreme conditions. A journey at sea becomes a logical extension of this goal. His choice of vehicle is the trawler *Norlantean*, and the reader is sent to steam across the open ocean feeling as seasick as the writer while the 70-year-old engines struggle with a force-12 storm. After a curious sequence of naming of parts, the ship is re-equipped with the collective personality of its occupants in this peculiarly indoor tale. This is not a conventional travel adventure, despite the physical extremes. All the action occurs in restricted spaces, not least the net that confines the fish, but also O'Hanlon's claustrophobic bunk, the cramped galley, the fish gutting room, and the icy hold.

The main stars are the fish and the fisheries scientist who studies them. In *Trawler* we learn fragments about the life histories of rattails, hagfish, squid, angler fish, lumpsuckers, Greenland halibut, and the trawler's main prey, redfish. Indeed, only fragments are known about the biology of many of these species. We also discover that the nets have to be shot a kilometer deep or more to catch anything. The skipper of the *Norlantean* is in debt to the tune of £2 million, hence his urgency to set sail whatever the sea conditions. Nevertheless, the waste is pitiful: even trawlermen will eat fish, especially a fat haddock, but they cannot consume all the nonquota fish they catch and these (dead on arrival at the surface) are flung to the kittiwakes and gannets. Further, on landing in Shetland, the catch will be exported because the British prefer cod and haddock, for which this skipper has no quota, and which in turn now have to be imported from remote fisheries.

Trawler
A Journey Through the North Atlantic
by Redmond O'Hanlon

Hamish Hamilton, London, 2003. 352 pp. £20. ISBN 0-241-14014-5. Paper, Penguin, London, 2004. £7.99. ISBN 0-140-27668-8. Forthcoming from Knopf, New York. ISBN 1-4000-4275-5.

To survive economically, each time he goes to sea *Norlantean*'s skipper has to net in excess of 70,000 pounds of fish. To hunt successfully, he must wield considerable interdisciplinary expertise. His many tasks include integrating data on distributions of fish species in three dimensions, population sizes, seasonality, diversity, average weight, gender and reproductive condition as well as directing the engineer, navigating the trawler, manipulating banks of electronic gear, and being chief psychiatrist for the crew. By contrast, the author is profoundly apologetic about his own stupidity and ignorance. As a result, *Trawler* is not a technical account—the extreme conditions of the journey probably rendered the landlubber author incapable of taking detailed notes or interviewing the crew in depth. But the reader nevertheless receives a sense of the sheer gut-wrenching endurance needed to work on a trawler and gains considerable sympathy for the sleepless, and consequently somewhat deranged, trawlermen.

Given the huge financial debts, the unnervingly high risk of drowning, and the evident lack of romantic glamour despite the dangerous nature of the work, one might wonder why people are still attracted to this terrible job. The answer seems to be that industrial fishing still offers employment, when little else in many remote coastal communities does. But at what cost?

As we continue industrial scale operations, many fisheries around the world are at the brink of collapse. It is paradoxical that fishing still pays, as Daniel Pauly noted in his recent talk at the Royal Society (21 July). That it does is due to huge national subsidies (e.g., approximately $2.5 billion for North Atlantic operations). Consequently, many global fisheries overshot their economic threshold some time past, but the subsidies have allowed fishing to continue until the ecological threshold has now also been exceeded. Hence, the lack of recovery of cod on the Grand Banks. Another consequence of the subsidies is that energy efficiency is plummeting—on average, for every metric ton of fuel consumed, only 1.5 metric tons of fish are harvested. Some fisheries are orders of magnitude worse; for example, catching a metric ton of shrimp may cost 100 metric tons of fuel. The worst offenders in the current devastation of the oceans, and those most resistant to reform, are members of the European Union. The EU "flagship" is the 14,000-metric-ton Irish factory trawler *Atlantic Dawn* (see figure), now helping to clear West African seas of fish. Not far behind are fleets from Japan and the former Soviet Union. More optimistically, Pauly suggests that the looming energy crisis will bring some sanity into this spiral of inefficiency.

That the world's fisheries are hanging on the brink of the abyss is not one of O'Hanlon's crazy hallucinations—and before fish become a culinary hallucination, the wealthy nations of the world need to act urgently to conserve what remains.

–CAROLINE ASH

CREDIT: HARALD M. VALDERHAUG

PUBLIC HEALTH

Whatever Happened to the U.S. AIDS Epidemic?

Harold Jaffe

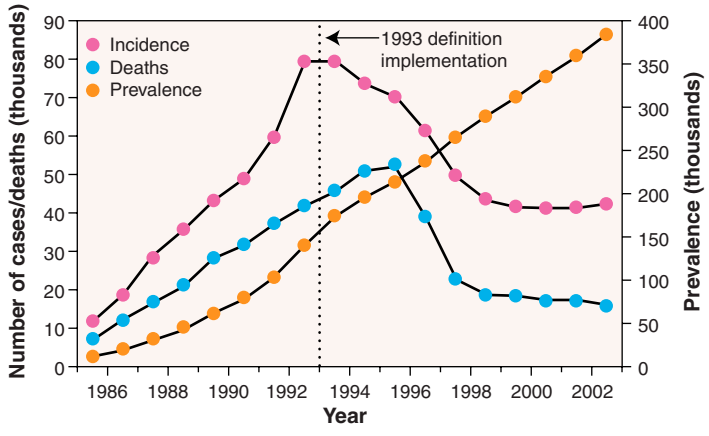
Although more than one-third (36%) of Americans believe AIDS is the "most urgent health problem facing the world today," ranking second behind cancer (41%) (*1*), concern about HIV/AIDS in the United States has been falling. In national surveys, the proportion of Americans who consider HIV/AIDS to be the "most urgent health problem facing this nation today" has decreased from 38% in 1997 to 17% in 2002" (*2*). The Centers for Disease Control and Prevention's (CDC) budget for domestic HIV/AIDS programs increased by only 5% from 2001 to 2004, less than the rate of inflation (*3*).

Enhanced online at www.sciencemag.org/cgi/content/full/305/5688/1243

Some of the decreasing interest in the domestic epidemic is understandable. With the increasing availability of highly active antiretroviral therapy (HAART), annual AIDS cases and deaths have fallen dramatically (see the figure). AIDS is now viewed by many as a chronic disease for which survival can be measured in years rather than months. As the profile of persons with AIDS has gradually shifted from white middle-class gay men to poor African-American and Hispanic residents of the inner city and rural South, and as AIDS "celebrity deaths" become fewer, the general public appears to find the epidemic less alarming. Yet there are still reasons for concern.

The Problem

Since the epidemic was recognized in 1981, it has killed more than half a million Americans, a total exceeding all American combat-related deaths in all wars fought in the 20th century. Despite great advances in treatment, HIV/AIDS is the second leading cause of death in African Americans between the ages of 25 and 44 years. The number of Americans living with AIDS also continues to rise and is now approaching 400,000 (see the figure). Because of variability in state reporting laws and the difficulty in distinguishing between recent and long-standing infection, precise national HIV incidence data are not available. However, the CDC estimates that about 40,000 Americans become infected each year (*4*). This figure is not believed to have changed over the last decade. The mean annual expenditure for care of an HIV-infected patient in the HAART era is estimated to be about $18,000 (*5*).



Number of AIDS cases, deaths, and persons living with AIDS in the United States. Numbers are adjusted for reporting delays. All surveillance data are from (*23*).

A major challenge to prevention is to increase the number of persons who know their HIV infection status. Without this knowledge, infected persons cannot know they may be transmitting the virus to others and will not receive HIV treatment and care. Yet of the estimated 850,000 to 950,000 infected Americans, about a quarter are unaware of their infection (*6*). Even when persons do seek testing, it is often late in the course of their infection. For example, during 2000 and 2001, 37% of persons diagnosed with HIV either had AIDS at the time of their first positive test or developed an AIDS-defining condition within a year of that test (*7*). To some extent, this problem reflects the reluctance of health care providers to offer routine testing to persons at risk for HIV infection or living in high-prevalence areas. Early in the epidemic, there was strong opposition to HIV testing because of perceptions that the test was inaccurate and the confidentiality of results could not be maintained (*8*). Many providers also considered the requirements for extensive pretest counseling burdensome. Moreover, because treatment was not available, there was little incentive to learn one's infection status.

Although the proportion of men who have sex with men (MSM) among reported AIDS cases has decreased, this population still accounts for the largest number of persons with AIDS. Further, in the 30 states with long-standing reporting of HIV infection, diagnoses among MSM increased 17% from 1999 to 2002, while remaining stable in other risk groups. Outbreaks of infectious syphilis in MSM, about half of whom are HIV-infected, indicate ongoing high-risk behavior. The continuing HIV epidemic in MSM remains a prevention challenge, with no easy answers. Many factors may be contributing to these behaviors (*9*). One likely explanation is that HIV/AIDS is no longer viewed as a fatal disease. Older MSM may also be suffering from "prevention fatigue," meaning that they are simply tired of hearing the same prevention messages. For younger MSM, the lack of apparent illness in peers along with the belief that HIV/AIDS was only a problem for a past generation may contribute to risk-taking behavior. Other factors contributing to unsafe sex may include the use of recreational drugs, particularly crystal methamphetamine (*10*) and easy access to anonymous partners through the Internet (*11*).

Among African Americans, the epidemic poses particular prevention challenges. Overall, AIDS case rates are 10 times higher in African Americans than in white Americans. Reasons cited for these high rates include poverty, substance abuse, increased rates of other sexually transmitted diseases that facilitate HIV transmission, and lack of access to and utilization of health care. Particularly hard hit have been African-American women and youth, who account for about two-thirds of AIDS cas-

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es in women and teenagers, respectively. Many of the young women are being infected by older male sex partners. Bisexual men may also be playing a role in transmission to women. In one study of HIV-infected MSM, 34% of African Americans acknowledged having sex with both men and women as compared with 13% of non-Hispanic whites (*12*) .

Some Solutions

To address some of the prevention challenges, CDC announced a new public health initiative in 2003: *Advancing HIV Prevention: New Strategies for a Changing Epidemic* (*4*). Much of the initiative is focused on increasing knowledge of infection status by making HIV testing a routine part of medical care and providing new models of testing outside of medical settings. The initiative also emphasizes prevention programs for infected persons, including strategies to decrease mother-to-child HIV transmission. In the prenatal setting, for example, voluntary "opt-out" testing (notification that an HIV test will be included in a standard battery of prenatal tests unless refused) is now a recommended approach to prevent perinatal transmission (*13*). Pretest counseling need not be extensive (*14*).

A key technical advance for increasing knowledge of infection status has been Food and Drug Administration (FDA) approval of a rapid HIV antibody test that can be performed outside the laboratory and provide results in about 20 minutes (*15*). The use of this test is now being evaluated for persons receiving care in medical settings, such as emergency departments, as well as in nonclinical settings, such as mobile outreach vans. Persons with negative results can be told they are not infected. Those with positive results are told that they are likely infected and are asked to return in a week or two for a confirmed result.

Progress in HIV prevention will also require identifying new prevention venues, such as correctional facilities. At any given time, about 2 million Americans are incarcerated in prisons or jails. At the end of 2001, 2.0% of state prison inmates and 1.2% of federal prison inmates were known to be HIV infected (*16*). Many other jail and prison inmates are at risk for infection upon release based on their histories of drug use or high-risk sex. In jails, where stays are typically only a few days, rapid HIV testing is feasible and can be linked to prevention and care services for those found infected. In prisons, where stays are longer, more comprehensive HIV prevention programs can be instituted. Making HIV prevention a priority in correctional settings will require both funding and a commitment from public health and correctional officials.

Advancing beyond the status quo may also require actions that have not been politically acceptable. For example, sharing of needles and syringes is the main route of HIV transmission among injection drug users, who still account for almost a quarter of newly reported persons with AIDS. However, access to sterile injection equipment is often limited by state laws that restrict sales of syringes, criminalize their possession, and limit the operations of needle and syringe exchange programs. Although exchange programs have been shown to reduce needle sharing (*17*) and are supported locally by city governments and community-based organizations, as well as internationally by the governments of many other industrialized countries, the use of U.S. government funds for these programs is prohibited. HIV prevention programs for injection drugs users should also include access to high-quality addiction treatment, along with prevention case management services for infected persons; such services are not always available or adequately funded.

The role of abstinence programs has also been politicized in the development of HIV prevention strategies. Abstinence, including interventions to delay the onset of sexual activity, clearly makes sense as a prevention strategy for youth, and has been shown to be effective in heavily affected countries, such as Uganda (*18*). However, the majority of American teenagers, over 60% in 2003, report that they have been sexually active by the time they are high school seniors (*19*). Additionally, the "abstinence until marriage" message has no meaning for gay and lesbian persons, for whom marriage is illegal in most of the United States. In contrast, prevention strategies emphasizing correct and consistent use of male condoms, a highly effective means to prevent HIV transmission (*20*), have been criticized (*21*).

New voices and community leadership to support HIV prevention are urgently needed. The dramatic upswing of HIV infections that occurred among MSM during the early 1980s was followed by an equally dramatic drop in incidence during the mid-to-late 1980s (*22*). This reduction occurred well before substantial federal or local funding for HIV prevention became available and almost certainly reflects prevention efforts within gay communities themselves. However, many of the leaders of those efforts have either died or are no longer active in HIV prevention. Although current activism largely has focused on access to therapy, more advocacy for prevention is critical. The message must be that prevention of HIV infection is of paramount importance, even though the infection is now treatable. Infected persons, individuals who know the burden of lifelong treatment with potentially toxic drugs, could be particularly credible spokespersons.

Similarly, more HIV prevention leadership is needed in the African-American community. Because of a variety of issues, particularly those related to racism, stigmatization, and homophobia, there has been some reluctance within this community to acknowledge the seriousness of the HIV/AIDS problem. For some, the epidemic may be just one more burden to bear. The black church and other faith-based entities, powerful social forces in the African-American community, can play critical roles in HIV prevention. Without political, community, and faith-based leadership, the problem will only become worse.

Americans should be proud that their country is now fully engaged in the global fight against HIV/AIDS. At the same time, however, we must ask ourselves why we, collectively, don't care more about the domestic epidemic. Thousands of young Americans are dying each year of a preventable infection.

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NEUROSCIENCE

In the Place Space

David K. Bilkey

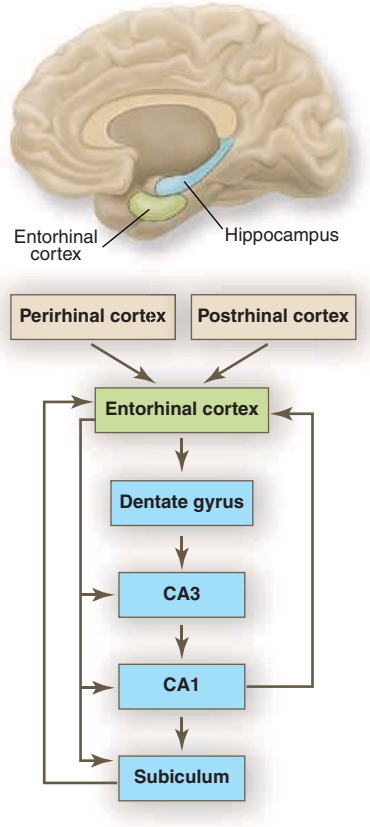
Where did I leave my car? Such questions remind us that spatial memory underlies our ability to move purposefully through the environment. The search for the neural foundations of this ability center on the hippocampus, a brain structure involved in the type of spatial memory that we use to navigate to a location hidden from view, such as a parking space. Two reports in this issue, by Fyhn *et al*. (*1*) on page 1258 and by Leutgeb *et al*. (*2*) on page 1295, provide fresh insights into how the hippocampus contributes to spatial memory.

When a rat is foraging freely in an open arena, the firing rate of many hippocampal neurons will be modulated by the animal's position in space. These neurons are known as "place cells," and the region in the animal's environment in which a particular cell fires is known as its "place field." Each place cell has its own place field, which usually covers about 10 to 20% of the current environment, and the cell is silent when the animal is outside this location (*3*). A network of place cells could thus represent the current environment, and the ensemble activity of the network could potentially encode the animal's own position in relation to distinctive features and events within that environment. Although rats don't often park cars, they have good spatial memory, and we assume that similar basic mechanisms underlie this ability in many different species, including humans (*4*).

The Fyhn *et al*. study (*1*) asks where in the brain place fields are built. Are they constructed within the hippocampus, or is the process completed in other "upstream" brain regions (see the figure)? Previous electrode recordings from upstream regions such as the entorhinal cortex have revealed that neural firing is only weakly modulated by the position of the animal. This implies that the hippocampus is able to construct a high-resolution representation of spatial location. Fyhn *et al*., however, have obtained data that cast doubt on this conclusion. They recorded specifically from the dorsocaudal region of the rat entorhinal cortex, which contains cells that project to the portion of the hippocampus where spatial firing is most prominent. They found that cells in this region encode almost the same amount of information about the animal's location as hippocampal place cells. In contrast, cells in other regions of the entorhinal cortex have poorer spatial specificity, explaining the conclusions of earlier studies. Fyhn *et al*. then showed that hippocampal lesions had minimal effects on the spatial firing of entorhinal neurons. Thus, the entorhinal cortex does not merely receive spatial information projected back from the hippocampus. Fyhn and co-workers also confirmed that cells in the cortical regions that provide major inputs to the entorhinal cortex responded minimally to the animal's location, supporting the notion that spatial representation is built in the entorhinal cortex.

So, if the representation of the animal's location is completed upstream of the hippocampus in the entorhinal cortex, what further processing takes place in the hippocampus and what is the contribution of its different subregions? Although the CA3 and CA1 hippocampal subregions differ from each other in terms of their anatomical inputs, their internal connectivity, and their involvement in behavior (*5*), their basic place field properties are similar. Furthermore, as we have seen, these place field properties resemble those in the entorhinal cortex. This is somewhat difficult to reconcile with the argument that the hippocampus performs further processing of the location representation generated in the entorhinal cortex. In a complementary study, Leutgeb *et al*. (*2*) now report that the difference between CA3 and CA1 (and probably entorhinal) activity is related to their encoding of the background information that we might call context.

Place fields are normally stable over repeated testing provided that the environment remains constant throughout the recording procedure. However, changing the environment between recording sessions is known to induce a "remapping" of place fields (*6*): Place fields either shift their firing location or switch their firing on or off within the modified environment. This phenomenon has been interpreted as a response to a change in context (*7*). Leutgeb *et al*. confirm that the ensemble of place fields in both CA1 and CA3 was stable when repeated testing was conducted without changing the recording environment. When the animal was recorded in identical arenas but in different rooms, however, the researchers found that CA3 cells displayed widespread remapping, whereas CA1 cells remained relatively stable. Then Leutgeb and colleagues compared the amount of remapping that took place when the shape of the recording arena was changed, but the room was not. Again, CA3 was remapped, but CA1 remained stable. However, a complete change in the environment in which both the room and the shape of the recording arena were altered induced remapping in both CA3 and CA1 hippocampal subregions. Leutgeb *et al*. then placed the animals into a new environment to determine how rapidly CA3 and CA1 cells developed a representation of the new setting. Whereas CA1 place firing was stable within the first few minutes of recording, the CA3 representation took



Where is my car? (**Top**) Spatial memory, for example, of where the car is parked, is encoded by the entorhinal cortex (green) and the hippocampus (blue) of the human brain. (**Bottom**) Shown are the principal connections between the entorhinal cortex and subregions of the hippocampus (blue rectangles). Regions such as the perirhinal and postrhinal cortex provide multimodal input to the entorhinal cortex where context-independent representations of the animal's location in space are generated. Context-dependent representations of location are then generated in the hippocampus.

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20 to 30 minutes to reach a stable state.

What do these findings suggest about spatial processing within the hippocampus? One possibility is that CA3 encodes the animal's location with reference to the current environmental context. This would be a useful extension to the coding scheme in the entorhinal cortex, where "place cells" appear to be relatively immune to changes in the environment (*8*). The context-dependent representation in CA3 might allow spatial memory to differentiate between different environments and so, for example, allow me to locate my car in the supermarket parking lot without interference from occasions when I parked it at the mall. But what about CA1? Leutgeb *et al*.'s finding that the pattern of activity in CA3 can change without affecting CA1 activity suggests that the CA1 region responds to direct inputs from the entorhinal cortex rather than to information routed through CA3 (*9*, *10*). But why would CA1 echo the entorhinal representation? One possibility is that CA1 melds information that was not explicitly examined by Leutgeb *et al*. into the spatial representation. Such information could include nongeometric features of the environment, such as odor or behavioral contingencies, or internal states such as hunger, thirst, or motivation. Alternatively, because remapping is known to take place in this region following manipulations of the spatial relationship between local and distal cues (*10*), CA1 may help to represent intercue associations. With these questions still waiting to be answered, it will be interesting to see how future studies gradually tease apart the components of the entorhinal-hippocampal memory system. This process will lead to a clearer picture of how neural networks in these regions interact during memory storage and retrieval. Now, where did I leave my keys?

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BEHAVIOR

Sweet Revenge?

Brian Knutson

You've been waiting in line in traffic for what seems like hours, when a red sports car whips past on the shoulder. Eventually, the sports car creeps back into view—the driver has run out of shoulder and signals to be let in. Instead of giving way, you stare ahead and accelerate, inching dangerously close to the bumper in front of you. After squeezing back the intruder, you can't help but notice a smile creep onto your face.

Judges worry, whereas filmmakers delight, in the fact that revenge feels good. Evolutionary theorists argue that such an "eye-for-an-eye" strategy makes sense, preventing future damage to one's self or kin (*1*, *2*). Yet, in cases ranging from inconsiderate drivers to Nazi war criminals, even unrelated onlookers seem highly motivated to seek revenge, often in spite of personal cost. From the standpoint of self-interest, punishing those who violate the interests of strangers—a form of revenge called altruistic punishment—seems irrational. Enter de Quervain and colleagues (*3*) on page 1254 of this issue, who offer an alternative explanation—instead of cold calculated reason, it is passion that may plant the seeds of revenge.

Using an elegant laboratory task designed to elicit acts of revenge among human volunteers, de Quervain and colleagues appear to have captured this complex emotional dynamic of schadenfreude with a positron emission tomography (PET) camera. During the task, subjects played games involving real money with a series of different partners. In each interaction, subjects chose to give their partners money, which was then quadrupled. Next, partners who received the money had a chance to reciprocate, or to pay back half to the subject. If partners decided not to reciprocate, or defected, subjects could choose to administer punishment. At this point, their brains were scanned.

De Quervain and coworkers first asked whether choosing to punish a defector would recruit brain circuits implicated in reward processing. They found that when subjects administered a monetary punishment to defectors, a subcortical region of the brain called the striatum increased its consumption of oxygen (that is, was "activated"). The investigators interpreted this to indicate that punishing a defector activates brain regions related to feeling good about revenge rather than brain regions related to feeling bad about having been violated. Indeed, these striatal foci lie near brain areas that rats will work furiously to stimulate electrically (*4*). The investigators then asked whether the striatum would be activated even when administering the punishment carried a personal cost. They found that the striatum was still activated when subjects chose to administer punishment at a personal cost, as was a region in the medial prefrontal cortex (MPFC) that has been implicated in balancing costs and benefits (*5*). Although these findings suggested a connection between striatal activation and the satisfaction one might derive from punishing a defector, they do not establish a directional relationship between the two. Thus, in a clever internal analysis, the investigators observed that the degree of striatal activation during no-cost punishment predicted the extent to which subjects chose to punish at a personal cost (that is, under less satisfying conditions). This finding suggested to the investigators that striatal activation indexed subjects' anticipation of satisfaction, rather than satisfaction per se.

"Go ahead, make my day." Dirty Harry succinctly informs a norm violator that he anticipates deriving satisfaction from inflicting altruistic punishment.

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These findings fit a fresh piece into the rapidly expanding puzzle of reward processing as revealed by brain imaging. Ironically, punishment of defectors in this study activated the same regions (that is, striatum and MPFC) that were activated when people rewarded cooperators in a recent functional magnetic resonance imaging (fMRI) study (*6*). These seemingly diametrically opposite social behaviors are united by a common psychological experience—both involve the anticipation of a satisfying social outcome. As presaged by comparative research (*7*), humans also show increased striatal activity during anticipation of nonsocial rewards such as monetary gains (*8*) and pleasant tastes (*9*). Together, these findings imply that for certain parts of the striatum, it's the feeling that counts.

As with any compelling study, the findings raise additional questions for future research. Although PET measures absolute metabolism (and can even provide neurochemical information), its spatial and temporal resolution are limited (in this case, to

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15 mm^3/min). Thus, although they were able to visualize activation at the head of the caudate, the investigators may not have been able to track activity in the smaller ventral part of the striatum—the part most directly implicated in motivation (*10*). Fortunately, event-related fMRI can resolve activity in smaller regions (~4 mm^3) on a second-to-second basis (*11*). Techniques like this may enable future investigators to make even more specific observations regarding when and where activation occurs during altruistic punishment. Second, while the present PET study of defectors included male subjects, the aforementioned fMRI study of cooperators included females. Future research will undoubtedly need to explore which social interactions most powerfully motivate men compared with women (as well as members of different social groups). Regardless, the findings do powerfully illustrate the importance of considering proximal emotional mechanisms in brain imaging studies of social behavior (*12*). The new results also suggest that, depending on social learning, some of the same emotions that bring us together can also break us apart.

The findings of de Quervain *et al*. also chip yet another sliver from the rational model of economic man. In fact, their subjects illustrated at least two types of irrationality: reacting on the basis of emotional considerations and spending costly personal resources to ensure that defectors got their due. Beyond providing a compelling justification for adding social justice concerns to existing economic models, the findings serve as a harbinger of future "neuroeconomic" studies that strive to descriptively reconstruct these models using neurobehavioral data. One can imagine the new models accommodating both "passionate" and "rational" forces, as well as specifying when and how they come together to influence individual choice.

Back in traffic, brake lights flare ahead. You realize that your smile was short-sighted. Your car skids to a halt. Fortunately, the smile didn't cost a pile-up. This time.

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GEOSCIENCE

What Caused the Great Lisbon Earthquake?

Marc-André Gutscher

On 1 November 1755, as worshippers in Portugal and southwestern Spain were gathered for mass on All Saint's Day, a tremendous earthquake struck, toppling many churches and killing about 60,000 people (*1*, *2*). Many churchgoers were killed, sparking a lively debate among philosophers about divine justice. Recent studies have shed light on what caused the earthquake and what the seismic future of the region may be.

The Great Lisbon earthquake had an estimated magnitude (*M*) 8.7. It triggered a 5- to 10-m-high tsunami and caused many casualties in Europe and northwestern Morocco (*2*). In this region, the African plate pushes toward the northwest against southern Iberia at a rate of 4 mm/year (see the figure, left panel). But the plate boundary off southern Iberia is not well defined (*3*), and the source of the Great Lisbon earthquake has remained elusive (*2*). Indeed, it has been difficult to find a simple plate-tectonic model that explains all geological observations in the region (*4*, *5*).

During the past 15 million years, crustal thinning and extension have produced a deep marine basin in the West Alboran Sea (western Mediterranean), while shortening and thrusting continued in the horseshoe-shaped Betic and Rif mountain belts (see the figure, left panel) (*4*, *5*). A popular model concluded that this region was a prime example of "delamination" (breaking off of a deep mantle root following continental collision) (*4*). However, new data increasingly support eastward subduction beneath the Straits of Gibraltar (see the figure, right panel) (*5*, *6*). Tomographic cross sections of the Earth show cold, dense material—a slab of oceanic lithosphere—descending from the surface to depths of nearly 700 km (*6*). The chemistry of 15- to 5-million-year-old volcanoes in the Alboran Sea shows that they were formed in an arc setting (like that of arcuate island chains in the West Pacific landward of the subduction zone) (*7*).

Overall, the movement of tectonic blocks in the southern Iberia region is best explained by a model of slab retreat (rollback) during subduction, causing extension in the region behind the subduction zone (*5*, *6*, *8*). The southeastern limit of deformation in this back-arc region appears to be a major north-east trending strike-slip fault across the West Alboran Sea (*9*). This fault emerges on land in northeast Morocco, right where the Al Hoceima earthquake ($M = 6.3$) struck on 24 February 2004, causing nearly 600 deaths.

One big question remains. Is the subduction system still active, and does it pose a seismic risk? New evidence supports continued activity. Numerous active mud volcanoes have been identified and sampled in the Gulf of Cadiz (*10*). These features indicate ongoing dewatering processes, which are widespread in accretionary wedges (compressed sediment piles formed at subduction zones, like piles of dirt in front of a bulldozer). Marine seismic data indicate active folding and thrusting of the youngest sediments (which are a few thousand years old) at the outermost edge of this accretionary wedge (*11*). Marine heat flow data are also indicative of active subduction (*12*).

An active subduction zone off southern Iberia poses a long-term seismic risk and is a likely candidate for having produced the Great Lisbon earthquake in 1755. However, no instrumentally recorded subduction interface earthquakes have been recorded in the Gulf of Cadiz. Hence, subduction has either ceased, is active and aseismic, or is active but the seismogenic fault zone is locked. The latter interpretation seems most likely. In this case, the Gibraltar subduction would resemble the Nankai and Cascadia subduction zones, which are characterized by a large locked zone and have a recurrence time of 100 to 1000 years for great earthquakes.

Additional clues can help to pinpoint the likely location of the Great Lisbon earthquake. The generation of a strong tsunami implies a source region mostly at sea. The tsunami wave can be modeled and compared to historical observations (*2*). A record of past great earthquakes exists in the abyssal plains off southwest Iberia in

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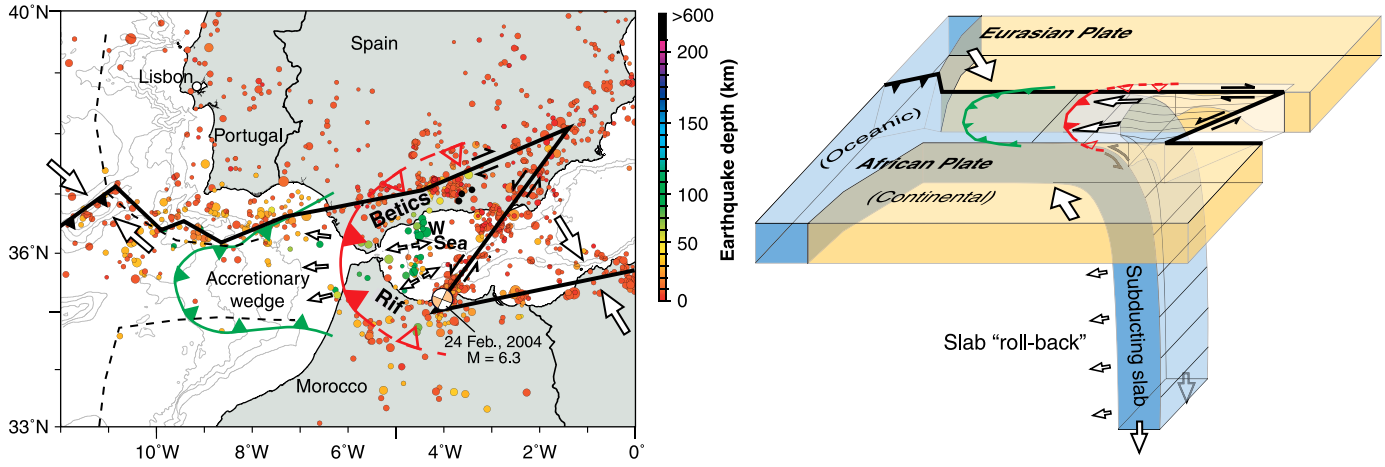

Seismicity and tectonics. (Left) Simplified tectonic boundaries and seismicity (from U.S. Geological Survey PDE Catalog 1980–2004, $M > 3$) in the southern Iberia region. Arrows indicate relative motions of major plates and tectonic blocks. Bathymetric contours are shown at 1000-m intervals (from General Bathymetric Chart of the Oceans 1-min digital Atlas). The dashed line shows the inferred limit between continental and oceanic lithosphere. **(Right)** Three-dimensional block diagram indicating sinking and roll-back of oceanic lithosphere belonging to the African Plate.

the form of coarse-grained, sandy "turbidite" deposits laid down by submarine gravity slides during great earthquakes (*13*). These deposits suggest that events of the magnitude of the Great Lisbon earthquake occur periodically at ~1000- to ~2000-year intervals.

As the 250th anniversary of this greatest natural disaster in recorded European history approaches, the Gulf of Cadiz has become the target of a concerted international effort, supported by the European EuroMargins Program. Five oceanographic cruises are planned between summer 2004 and 2005. Three new proposals have been submitted to the Integrated Ocean Drilling Program to search for clues beneath the sea floor. Together, the new studies may help to unlock the secrets of this region's past and its likely future.

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GEOSCIENCE

Tidal Triggering Caught in the Act

Ross S. Stein

The lunar tides beat our entire planet, rhythmically stressing and relaxing every geological fault twice daily. These tiny stress changes may trigger small shocks on faults critically stressed for failure in future large earthquakes. Tantalized by this possibility, scientists have long searched for earthquakes triggered by tides, but the results have been, at best, equivocal. Tidal triggering does occur beneath some active volcanoes and mid-ocean ridges (*1*), and several studies report triggering of extensional and thrust earthquakes (*2, 3*). Yet strike-slip earthquakes, which are by far the most common, have shown little or no tidal influence (*2, 4*). In a recent paper in *Earth, Planets and Space*, Tanaka *et al.* (*5*) provide powerful insights into how tidal triggering works on strike-slip and thrust faults.

The stress imparted by earthquakes strongly influences the occurrence of subsequent earthquakes, such as aftershocks and successive main shocks (*6–8*). Seismicity rates increase where the Coulomb stress is calculated to rise (increased shear and unclamping), and generally drop where the Coulomb stress is calculated to decrease, a phenomenon most evident among strike-slip earthquakes. If, then, stress governs seismicity, why can we not more readily see a seismic response to the ubiquitous and predictable tides?

Stress magnitude is one answer. Typical earthquake-induced stress changes are about 1 to 10 bars, whereas the tidal Coulomb stresses are about 0.01 bar. The tidal effect is thus much weaker and might lie below a threshold. Frequency is another answer. Theoretical arguments (*9*) and laboratory evidence (*10*) suggest that the tidal oscillations are too brief to nucleate abundant earthquakes. Either way, if the tides only subtly influence seismicity or do so only near magma chambers, they are all but useless as a seismic sentinel.

Tanaka *et al.* (*5*) find that earthquakes are triggered by the tides only when the tidal stress adds to—that is, acts in the same direction as—the regional tectonic stress. Nearly all previous studies sought for an increased rate of earthquakes when the tidal stress is high or rising. In a sense, Tanaka *et al.* reframe the tidal triggering hypothesis in terms of the tidal stress azimuth rather than its phase. Reckoned this way, up to 10% of earthquakes are tidally triggered, an unexpectedly high percentage. Such a relationship had been predicted (*9*) but not demonstrated. Perhaps the biggest surprise is that tidal triggering is more common in Japan's tectonic regions than in its volcanic sites (*5*).

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The conclusion of Tanaka *et al*. rests on a two-part analysis, the first step of which appears decidedly tenuous. In one hundred 1° by 1° regions covering the Japanese archipelago, they compute the azimuth of the tidal compressional stress for 90,000 earthquakes, normalized by the tidal compressional stress for the same earthquakes but with randomized occurrence times. Tidal triggering is identified when the number of earthquakes departs from a uniform distribution. Tanaka *et al.* find tidal triggering in 13 regions. But at the 90% confidence level used in their analysis, 10 out of 100 regions should exhibit tidal triggering just by chance. An excess of three does not constitute causality.

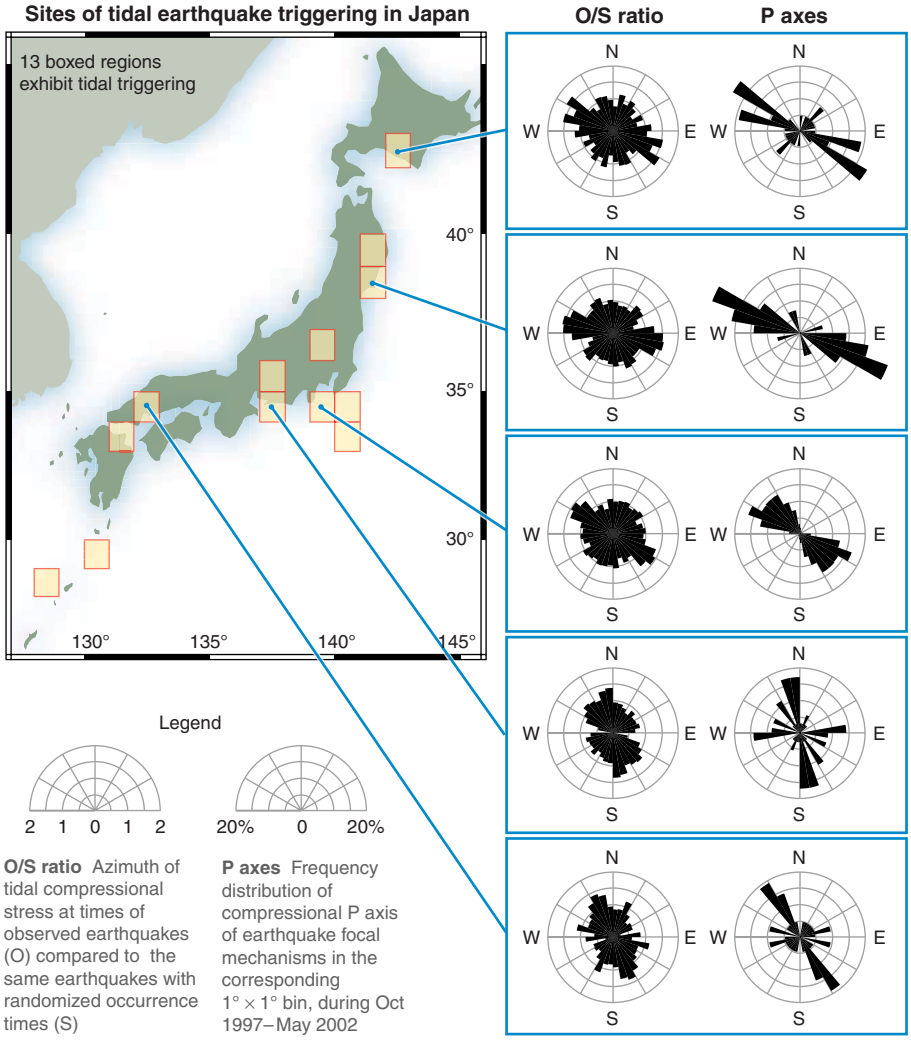
Undaunted, the authors next compare the azimuth of tidally triggered shocks to the azimuth of tectonic compression for the 10 of the 13 regions where this is possible. Suddenly, a long-sought signal emerges from the noise: a correlation between the peaks in the tidal and tectonic compression directions (see the figure).

Tanaka *et al.* also shed light on the Coulomb stress analysis of earthquakes. In doing so, they reveal why a widely used technique for studying earthquake triggering (*11*)—resolving stress changes on planes optimally oriented with respect to the net regional and earthquake stress—has worked so well. It is because earthquakes are triggered by amplifying the tectonic stress under which faults operate. A large stress change that would force a fault to slip in a direction other than the one in which it has evolved has little effect, whereas a tiny nudge in its natural slip direction can nucleate an earthquake. The results reported by Tanaka *et al*. also upend arguments that the high rate of tidal oscillations all but precludes triggering (*12*). Given that most shocks in Japan are thrust or strike-slip, they also challenge arguments that triggering cannot be detected in strike-slip regimes.

The Achilles' heel of the analysis by Tanaka *et al.* is why the tidal effect is evident in only 13% of the Japanese archipelago. The authors suggest that regions must reach a critical stress before the small tidal increments can trigger earthquakes. They support their claim by arguing that large shocks have preferentially struck regions exhibiting tidal triggering (*3*). But there are other plausible explanations.

First, the 13 regions could be subject to unusually strong tides. Tanaka *et al.* should therefore test whether the seismicity rate is proportional to the tidal phase when the tidal and tectonic stresses align. Second, faults might need to be uniformly oriented for tidal triggering to be detectable. Tidal triggering is identified in only one region with a complex stress and faulting pattern. Third, the 13 regions could have unusually low fault friction. To test this hypothesis, the authors should invert for the azimuth of the tectonic stress rather than plot the P axes. The latter represent the principal compression only if fault friction is low, because antithetical faults are then orthogonal to each other and share the same P axes. For high fault friction, antithetical faults form at acute angles to the principal compression direction, and their P axes would diverge.

Whether the study by Tanaka *et al*. proves to be a breakthrough depends on what happens next. Reproducing the results in California and Taiwan would strengthen if not cement the case. Examining cases with unusually large tidal stress changes due to ocean loading will test whether the oscillatory nature of tidal stress—rather than its small magnitude—inhibits triggering (*13*). Finally, Tanaka *et al.* should set up a formal forecast to see if large earthquakes strike the 13 regions at a higher rate than strike the rest of Japan. If so, then the dream of tidal monitoring of earthquake hazard could yet come true.



Tidal pull on Japan's shocks. Tanaka *et al.* (*5*) find that earthquakes are triggered by the tides when the tectonic stress, represented here by the compressional P axes of focal mechanisms, aligns with the tidal stress. Compare the left and right rose diagrams in each blue box; all shown are correlated at the 90% confidence level. But there is a catch: Just 13 of 100 regions exhibit tidal triggering, only slightly above the 90% confidence level. For the full data set, see the supporting online material.

CREDIT: ADAPTED FROM (*5*)

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www.sciencemag.org/cgi/content/full/305/5688/1248/DC1
Fig. S1
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SCIENCE AND POLICY

AAAS R&D Report Sees Sharp Rise for U.S. Security Spending

Confronted by continuing global instability and record federal deficits, the U.S. Congress is moving toward a 2005 budget that would sharply raise research and development spending for security initiatives while holding it steady or cutting it in most other areas.

Kei Koizumi, director of the AAAS R&D Budget and Policy Program, reported this month that the U.S. Congress and President George W. Bush already have approved a 7.1% increase for research and development in the Department of Defense (DOD), raising the appropriation $4.7 billion to a record $70.3 billion. The House of Representatives would raise R&D spending for the Department of Homeland Security by 19.3%, while the Senate would increase the investment by 17.2%.

But in an interview, Koizumi said that areas such as energy, climate, transportation, space exploration, and the National Science Foundation (NSF) are facing cuts. The House R&D budget for the National Institutes of Health (NIH) would rise 2.6%, but a significant portion of that is made up by an increase in biodefense research. Excluding NIH, funding for all nondefense research and development would decline 2.1% under the House plans.

"Clearly, the big winners are defense and homeland security," Koizumi said of the budget process so far. "Within defense, the big priorities are missile defense and development and engineering work for some weapons systems that are in the pipeline. But Congress also did find money to boost Department of Defense support of research."

The R&D Budget and Policy Program has emerged as an authoritative source of budget information over the last 30 years, and today, Koizumi's reports are watched closely on Capitol Hill and frequently cited in news reports. "I always say his analyses are essentially the gold standard for science budgeting," said Bob Palmer, minority staff director for the House Science Committee. The analyses on R&D appropriations are updated regularly on AAAS's Web site at www.aaas.org/spp/rd/.

Before Congress recessed in July, the House had approved 10 out of a total 13 appropriations bills for the budget year beginning 1 October, but had taken no vote on bills involving NIH, NASA, NSF, and other big R&D agencies. The Senate had completed action only on the DOD appropriation bill.

Kei Koizumi

The big winner within DOD is the agency that oversees the controversial missile defense system; its development budget will rise 16% to $8.8 billion. At the Department of Homeland Security, both the Senate and House would increase funding for shipping container security, air cargo security, and biowarfare countermeasures, among other projects.

But because Congress has set strict budget guidelines for 2005, Koizumi said, the Senate will have limited flexibility to modify the House R&D plans.

"While the Senate total for R&D spending could be higher than that approved by the House, there's just no room to make it very different," he said. "So the Senate could give an increase to NSF, for example…but in order to do that, they're going to have to find cuts somewhere else. And that makes the Senate's job very difficult."

Indeed, the budget decisions carry such political risk that Congress may wait until after the November elections to complete its work on the budget, Koizumi said.

If something close to the House budget prevails, President Bush's high-profile plans to put astronauts back on the moon and for the first time on Mars would be effectively frozen. And it is likely to mean fewer successful grant applications and a slowdown in some projects at agencies like NSF and NIH.

NIH, between 1998 and 2003, had been getting 15% more every year as part of a policy to double its budget; while the 2.6% House proposal for 2005 is in line with increases granted in the mid-1990s, it would be more than offset by the projected 3.5% inflation rate in the cost of doing biomedical research. Koizumi said some biomedical interests had pushed for a 9 to 10% increase in 2005 "to maintain the momentum of discovery."

HIGHER EDUCATION

New AAAS Center to Advance Careers in Science

The Alfred P. Sloan Foundation has awarded AAAS a 3-year, $400,000 grant to establish a new center that will provide consulting services to universities and colleges seeking to increase the participation of U.S. students, especially women and underrepresented minorities, in science and engineering.

Daryl Chubin, a national expert on expanding and diversifying the science and engineering workforce, has joined AAAS as the director of the new Center for Advancing Science and Engineering Capacity. Chubin has served in the White House Office of Science and Technology Policy and has published eight books and numerous policy reports, articles, and commentaries.

"By pulling together what we now know and setting a research agenda for the future, this center will surely help multiply the impact of the many efforts going on around the country to increase participation in science by members of underrepresented groups," said Alan I. Leshner, AAAS's chief executive officer and executive publisher of the journal *Science*.

Chubin "sees the big picture, and he knows the research base," added Shirley Malcom, director of Education and Human Resources at AAAS. "He understands the practical constraints that are inevitable as institutions try to prepare all students to live, work, and compete in a global and diverse workforce."

AAAS has taken a leadership role in recent years in identifying and shaping efforts to improve education in science, technology, engineering, and mathematics (STEM), and to recruit more students into those fields. In July, for instance, a day long AAAS conference in Washington, DC, looked at the lessons major universities

might learn from some nontraditional schools that have excelled at training women, minorities, and others for careers in information technology.

The need for the new Center for Advancing Science and Engineering Capacity can be traced to a shift in American culture described by AAAS President Shirley Ann Jackson in "The Quiet Crisis," a 2002 report for Building Engineering & Science Talent (BEST). While science and technology are increasingly critical to economic growth and innovation, student interest in the fields has not kept pace, wrote Jackson, a physicist and president of Rensselaer Polytechnic Institute. Data show that through the high-tech and medical research boom of the past 30 years, college enrollments in science and engineering have only held steady. In the past 15 years, for example, the proportion of women in computer sciences has declined.

Researchers have found that if minorities and women participated in the science and engineering workforce in numbers proportionate to their presence in the population, the workforce would be more diverse in composition and robust in talent for decades to come. But while many initiatives are under way, Chubin said, schools sometimes struggle with diversity. The picture was complicated by U.S. Supreme Court decisions last year which narrowed the range of tools that public universities can use.

"Universities need help fulfilling their commitment to a supportive environment for their core constituency—students," Chubin said in a recent interview. "The Center offers faculty and administrators the tools for becoming 'culturally competent'—welcoming and sustaining a diverse student body in STEM fields. Through technical assistance to programs, the Center can enhance what already works, retool what may be flagging, illuminate what is obscure, and scale up what is exemplary."

Drawing on expertise at AAAS and in the private sector, the Center will send small teams of consultants to individual schools to review and refine their programs in teaching and learning.

That model persuaded the Sloan Foundation to make the grant, with the belief that the Center can be self-supporting after 3 years. "We're convinced that the colleges and universities need the services in question," said Ted Greenwood, the project director who oversees Sloan's programs for women and minorities in science and engineering. "And we felt that AAAS had assembled a terrific team that has the skill to do this work."

Chubin comes to AAAS from the National Action Council for Minorities in Engineering, where he had served since 2001 as senior vice president for research, policy and programs. Before that, he had spent nearly 15 years in federal service, the last 3 as senior policy officer for the National Science Board at the National Science Foundation. In 1997, he was assistant director for Social and Behavioral Sciences (and Education) at the White House Office of Science and Technology Policy.

Earlier in his career, Chubin served on the faculty of four universities, including Georgia Institute of Technology. Since 1991, he has been an adjunct professor at the Cornell-in-Washington Program.

INTERNATIONAL

AAAS Youth Scientists Star at Beijing Fair

Nineteen top science students and four high school teachers in a AAAS delegation arrived in Beijing this month to find themselves at the center of a news media whirlwind. From the time the 3rd Asia-Pacific Economic Cooperation Youth Science Festival opened on 3 August until it closed on 9 August, newspaper and broadcast reporters expressed a keen interest in the American delegation. Students were quoted and photographed in stories in *China Daily, Beijing Today,* and *Beijing Youth Daily.* One was featured in a segment on CCTV, China's largest national television network.

But the interest was mutual. The Americans were surprised and fascinated by traditional Chinese medicine and by China's space program. And they bonded with their counterparts from China and around the Pacific Rim over concern about degradation of the global environment.

"Everyone is really starting to see the evidence of the greenhouse effect," said Liz Baker, 16, of Tucson, Arizona. "All of the kids I spoke to all seemed to feel that we need to stop what we're doing right now—stop pollution, stop destroying the forests."

Dong Zhengqi, a high school student from China's Inner Mongolia Autonomous Region, shared that view. "The environment around us is becoming worse and worse, so my research is about the environment," Dong said in a 4 August interview with the English-language *China Daily.* "I'd like to convey my ideas to my counterparts from all over the world and get to know their ideas on environmental protection."

AAAS's International Office organized U.S. participation in the festival, supported by the National Science Foundation. The delegation was led by Yolanda George, AAAS's deputy director of Education and Human Resources, and Clinton Turner Jr., AAAS's project manager for Science NetLinks.

APEC is an organization of 21 Pacific Rim countries and economic jurisdictions working to encourage growth, trade, and investment in the region. The science festival had been scheduled for last summer, but it was postponed until the deadly SARS outbreak was brought under control.

Nearly 900 science students, most of them still in high school, and nearly 350 teachers, researchers, and officials came from around the Pacific Rim to attend the event, which was hosted by China's Ministry of Science and Technology, the Ministry of Education, the China Association for Science and Technology, the Central Committee of the Chinese Youth League, and the city government of Beijing.

Three U.S students won top prizes in the Beijing competition: Vaishali Grover, 17, of Miami, Florida, took first place for developing a new marine paint with pineapple and papaya enzymes to replace the highly toxic paint now used to control the accumulation of marine organisms on ship hulls. Jeffrey Reitman and Sean Kshitij Mehra, both of Jericho, New York, shared a first-place award for nanotechnology research, including development of an industrial polymer to be used in lubricants for space machinery.

Adam Quade of Minnesota and Kels Phelps of Montana were second-place winners for their work on fluoride and tooth decay, and the medicinal value of the *Yucca glauca* plant, respectively.

"AAAS has a long history of cooperating with scientists in the Asia-Pacific region," said Shere Abbott, AAAS's chief international officer. "Providing an opportunity for the next generation of young scientists to understand the global culture of science and to build ties with their peers in these countries will strengthen international scientific cooperation in the region for years to come."

The same goal prompted NSF to underwrite the U.S. delegation to Beijing and to earlier APEC science festivals in South Korea and Singapore, said Frances Li, a senior staff associate in NSF's Office of International Science and Engineering.

"The festival meshes well with NSF's goal of fostering a diverse, globally oriented workforce of scientists and engineers," Li said. "NSF has funded AAAS to organize participation in the festival by a cross-section of bright students from around this country. NSF anticipates that as the alumni of these festivals mature into influential contributors to the science and engineering enterprise of the 21st century, the common bond of the festival experience will catalyze cooperative linkages around and across the Pacific Rim."

Chiral-Selective Aminoacylation of an RNA Minihelix

Koji Tamura and Paul Schimmel*

Aminoacylation of RNA is a first step in protein synthesis and thus was critical for the transition from the putative RNA world to the theater of proteins. All natural proteins are composed of L-amino acids. Aminoacylation of a dinucleoside monophosphate with the imidazolides of amino acids has shown that some aminoacylation products are enriched for the L-, some for the D-, and others for no specific enantiomer (*1*). Thus, the question of chiral selectivity in natural proteins remains unanswered.

To investigate chiral selection from a different perspective, we started with an RNA minihelix that recapitulates the domain within tRNA that harbors the amino acid attachment site. [The minihelix may have been the progenitor of modern tRNA (*2*, *3*).] Because contemporary systems use aminoacyl phosphate (mononucleotide) adenylates as intermediates for aminoacyl tRNA synthesis, we designed an aminoacyl phosphate oligonucleotide to hybridize to the 3′-end of the minihelix through a bridging oligonucleotide, thereby bringing together the activated amino acid and the amino acid attachment site. Thus, minihelix^{Ala} (based on the sequence of *Escherichia coli* tRNA^{Ala}), a bridging oligonucleotide, and 5′-[^{14}C]L-Ala-p-dT$_6$dA$_2$ (synthesized with 1,3-dicyclohexylcarbodiimide) were mixed together to achieve aminoacylation of minihelix^{Ala} (Fig. 1A) (*4*). (Deoxynucleotides were used for the aminoacyl phosphate oligonucleotide for reasons of technical convenience.) Denatured polyacrylamide gel electrophoresis (PAGE) under acidic conditions (pH 5.0) showed formation of a [^{14}C]L-Ala-minihelix in a template-dependent manner (fig. S1A). The efficiency of aminoacylation was ~15%, reduced largely by the hydrolysis of the aminoacyl phosphate oligonucleotide substrate and, to a lesser degree, of the aminoacyl minihelix product. To confirm that aminoacylation occurred at the 3′-end, minihelix^{Ala} was pretreated with $NaIO_4$ to oxidize the cis-hydroxyl groups (fig. S1B) (*4*). No aminoacylation was detected.

To further define the amino acid attachment site, we synthesized minihelix^{Ala} substrates with 2′- and 3′-deoxyadenosine (dA). The 2′-dA derivative was aminoacylated, but the 3′-dA substrate was not (fig. S1C) (3′-OH specific). Thus, spatial positioning of the aminoacyl phosphate was structurally constrained, so that chiral selectivity of the amino acid could be observed. We prepared 5′-[^{14}C]L-Ala-p-dT$_6$dA$_2$ and 5′-[^{14}C]D-Ala-p-dT$_6$dA$_2$ and observed that formation of [^{14}C]L-Ala-minihelix was preferred over that of [^{14}C]D-Ala-minihelix by a ratio of about 4:1 (Fig. 1B and fig. S2A).

We also tested both stereoisomers of Leu-p-dT$_6$dA$_2$ and of Phe-p-dT$_6$dA$_2$. A clear preference for L- over D-leucine (or phenylalanine) was observed (fig. S2B). No significant difference was seen when the spontaneous hydrolysis of 5′-[^{14}C]L-Ala-p-oligonucleotide versus 5′-[^{14}C]D-Ala-p-oligonucleotide was compared, either in the presence (the system with periodate oxidized minihelix was used to prevent aminoacylation) or absence of the bridging oligonucleotide. In addition, no significant difference in relative yields of L- versus D-aminoacyl-minihelix products was seen at 10, 20, or 30 min over the course of the reaction (fig. S2A). Thus, chiral preference appears to occur during aminoacyl transfer from the 5′-phosphate to the minihelix.

We also prepared RNA components with the opposite chirality and tested both L- and D-amino acids. Natural RNA molecules contain exclusively D-ribose. We synthesized the aminoacyl phosphate oligonucleotide, bridging oligonucleotide, and minihelix^{Ala}, which all contain L-ribose. Minihelix^{Ala}, bridging oligonucleotide, and either 5′-[^{14}C]L-Ala-p-dT$_6$dA$_2$ or 5′-[^{14}C]D-Ala-p-dT$_6$dA$_2$ (both containing L-deoxyribose) were combined and analyzed for aminoacylation of minihelix^{Ala}. Formation of [^{14}C]D-Ala-minihelix was preferred over that of [^{14}C]L-Ala-minihelix (Fig. 1C). The ratio of [^{14}C]L-Ala-minihelix to [^{14}C]D-Ala-minihelix was estimated as 1:3.6, about the reciprocal of that determined when we used RNA containing D-ribose.

With a chiral template, homochiral RNA synthesis has been demonstrated in the laboratory (*5*, *6*), suggesting that for RNA, once established, homochirality can be perpetrated. Our results raise the possibility that amino acid homochirality in proteins was determined during aminoacylation and that the selectivity (L or D) was determined in large part by the preestablished homochirality of RNA. RNA chirality may, in turn, have been influenced by prebiotic amino acids that were asymmetric catalysts for the synthesis of chiral sugars (*7*).

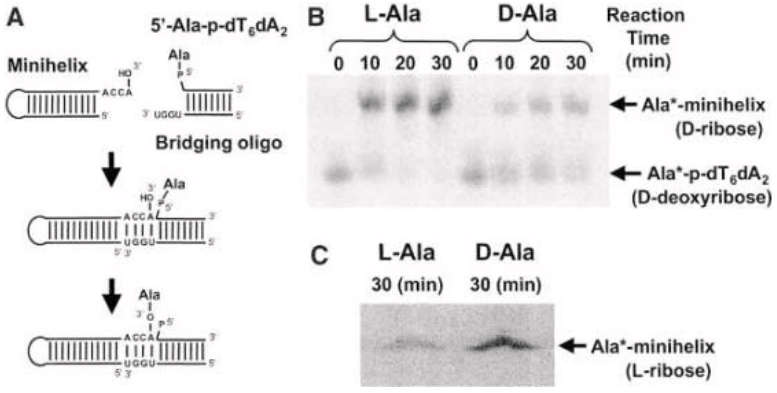

Fig. 1. (**A**) Scheme for aminoacylation with an aminoacyl phosphate oligonucleotide and a bridging oligonucleotide. (**B**) PAGE analysis of aminoacylation of the minihelix mixed with the bridging oligonucleotide and 5′-[^{14}C]-labeled-L- or D-alanyl-p-dT$_6$dA$_2$. (**C**) As in (B) but with L-ribose RNA.

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Materials and Methods
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The Neural Basis of Altruistic Punishment

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Many people voluntarily incur costs to punish violations of social norms. Evolutionary models and empirical evidence indicate that such altruistic punishment has been a decisive force in the evolution of human cooperation. We used $H_2{}^{15}O$ positron emission tomography to examine the neural basis for altruistic punishment of defectors in an economic exchange. Subjects could punish defection either symbolically or effectively. Symbolic punishment did not reduce the defector's economic payoff, whereas effective punishment did reduce the payoff. We scanned the subjects' brains while they learned about the defector's abuse of trust and determined the punishment. Effective punishment, as compared with symbolic punishment, activated the dorsal striatum, which has been implicated in the processing of rewards that accrue as a result of goal-directed actions. Moreover, subjects with stronger activations in the dorsal striatum were willing to incur greater costs in order to punish. Our findings support the hypothesis that people derive satisfaction from punishing norm violations and that the activation in the dorsal striatum reflects the anticipated satisfaction from punishing defectors.

The nature and level of cooperation in human societies is unmatched in the animal world. Humans cooperate with genetically unrelated strangers, often in large groups, with people they will never meet again, and when reputation gains are absent. Recent research indicates that strong reciprocity—the combination of altruistic punishment and altruistic rewarding—has been crucial in the evolution of human cooperation (*1*–*3*). People often reward others for cooperative, norm-abiding behaviors, and they punish violations of social norms (*4*, *5*). For thousands of years, human societies did not have the modern institutions of law enforcement—impartial police and impartial judges that ensure the punishment of norm violations such as cheating in an economic exchange, for example. Thus, social norms had to be enforced by other measures, and private sanctions were one of these means. Many norms are still enforced by private sanctions, even in contemporary Western societies. Such sanctions are altruistic if they involve costly acts that confer economic benefits on other individuals. If, for example, an individual sanctions a person who cheated in an economic exchange, the cheater's future interaction partners will benefit from this punishment because the cheater is now more aware that cheating will be punished. This knowledge is likely to deter future cheating (*3*).

Why do people punish violators of widely approved norms although they reap no offsetting material benefits themselves? We hypothesize that individuals derive satisfaction from the punishment of norm violators. Several sources suggest this hypothesis. First, recent models of social preferences (*6*–*8*) define utility functions that incorporate a motive to sanction violations of fairness and cooperation norms. These models predict actual behavior better than do models based on self-interested preferences, lending support to the idea that people are motivated to punish norm violations. Second, recent models of the evolution of human cooperation (*1*, *2*) indicate that altruistic punishment has deep evolutionary roots. This suggests that proximate mechanisms evolved that induce humans to bear the cost of punishing others. Because altruistic punishment is not an automatic response, such as the digestion of food, but rather is an action based on deliberation and intent, humans have to be motivated to punish. The typical proximate mechanism for inducing motivated action is that people derive satisfaction from the action. Most people seem to feel bad if they observe that norm violations are not punished, and they seem to feel relief and satisfaction if justice is established. Many languages even have proverbs indicating such feelings, for example, "Revenge is sweet."

A design to study the punishment of defectors. We examined the hypothesis that people derive satisfaction from the punishment of norm violations by combining an economic experiment involving real monetary payoffs with positron emission tomography (PET). Our hypothesis predicts that altruistic punishment is associated with the activation of brain areas related to reward processing. Single-neuron recording in nonhuman primates (*9*–*11*) and neuroimaging studies with humans using money as a reward medium (*12*–*16*) reliably indicate that the striatum is a key part of reward-related neural circuits. Moreover, if altruistic punishment occurs because the punisher anticipates deriving satisfaction from punishing, we should observe activation predominantly in those reward-related brain areas that are associated with goal-directed behavior. Single-neuron recording in nonhuman primates (*17*–*19*) provides strong evidence that the dorsal striatum is crucial for the integration of reward information and behavioral information in the sense of a goal-directed mechanism. A recent neuroimaging study also supports the view that the dorsal striatum is implicated in the processing of rewards that accrue as a result of a decision (*20*).

In our experiment, two human players, A and B, interact anonymously with each other (*21*). Both players know that they face a human player, and each of them is endowed with 10 money units (MUs). They can increase their income substantially if player A trusts B, and B acts in a trustworthy manner. More specifically, A makes the first decision. He can send his endowment of 10 MUs to B (case 1) or he can keep his endowment (case 2). If A trusts B and sends his endowment (case 1), the experimenter quadruples the amount sent so that B receives 40 MUs. At that moment, B has 50 MUs in total—his endowment plus the 40 units just received—and A has nothing. Then B has the choice of sending back nothing or half of the 50 MUs. Thus, if B acts trustworthily and sends back half, both players earn 25 MUs, but if B keeps all the money, he earns 50 MUs and A, who trusted B, earns nothing. In case 2, that is, if A does not trust B, both players keep their endowment of 10 MUs (*22*).

We hypothesized that if A trusts B, cooperation and fairness norms dictate that player B send back half the money. Therefore, if B is untrustworthy and keeps all the money, A interprets this as a norm violation, which we predict will evoke a desire to punish B. For

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this reason, A receives the option of punishing B by assigning up to 20 punishment points to player B (*23*). After player A is informed about B's action, A has 1 min to deliberate and decide whether he wants to punish B and, if so, how many punishment points to assign. The experimenter asks player A for his decision at the end of the minute. Because we are interested in the neural basis of punishment, we scanned A's brain during this 1-min period. In total, player A was sequentially matched with seven different subjects in the role of B, that is, A played the experiment described above seven times. Because both players can earn considerably more money if A trusts B, and B is trustworthy, A has a strong incentive to trust B; in fact, all but one subject in the role of A trusted B in all seven trials. Player A faced a trustworthy opponent in three of the seven trials, but B kept all the money in the remaining four trials. Because we are interested in imaging altruistic punishment, and to keep radioactivity as low as possible, we scanned those trials in which B kept all the money, because A is expected to have a desire to punish B only in those trials. During a 10-min break between trials, A answered questionnaires in which he assessed the fairness of B's action in the previous trial and his desire to punish B on a seven-point Likert scale. Fifteen healthy, right-handed male subjects participated in the role of player A in our experiment. Because we are interested in A's response to the abuse of trust, our analysis includes the 14 subjects who trusted B.

Predicted brain activations across treatments. Player A experienced four different treatment conditions in the four trials in which B kept all the money. These conditions generate the contrasts necessary to measure the activation of reward-related brain areas during the punishment period. In the condition termed "intentional and costly" (IC), B himself decides whether to keep all the money or to send back money. Thus, if B keeps all the money, he intentionally abuses A's trust. In addition, the punishment is costly for both A and B. Every punishment point assigned to B costs one MU for A and reduces B's payoff by two MUs. In the condition termed "intentional and free" (IF), B also decides about the transfer himself, but the punishment is not costly for A. Every punishment point assigned to B costs nothing for A, whereas B's payoff is reduced by two MUs. In a third condition, which we call "intentional and symbolic" (IS), B again makes the decision, but punishment has only a symbolic meaning. Every punishment point assigned to B costs neither A nor B anything. Thus, A cannot reduce the payoff to B in this condition. Finally, there is a condition called "nonintentional and costly" (NC) in which a random device determines B's decision, removing the responsibility for it from player B. Punishment is again costly for both A and B; A loses one MU and B loses two MUs per punishment point assigned to B (*23*). To control for sequence effects, the sequence of treatment condition was randomly determined.

These conditions enable us to test our hypothesis by computing the differences in brain activation across relevant conditions. We predict, in particular, that the contrast IF-IS activates reward-related brain areas after A's trust has been abused. We predict that A has a desire to punish B both in the IF and the IS conditions because B intentionally abused A's trust, but A cannot really hurt B in the IS condition. Thus, the purely symbolic punishment in the IS condition is unlikely to be satisfactory because the desire to punish the defector cannot be fulfilled effectively, and in the unlikely case that symbolic punishment is satisfactory, we predict that it is less so than punishment in the IF condition.

The satisfaction from punishing effectively may have various psychological sources. Subjects who do not punish may feel bad because the defector gets away unpunished and has a much higher payoff than they themselves have; in this case, effective punishment prevents a negatively reinforcing outcome. Alternatively, effective punishment may be perceived as just and subjects may feel good about this; in that case, punishment is associated with a positively reinforcing outcome.

The IF-IS contrast is ideal for examining the satisfying aspects of effective punishment because, except for the difference in the opportunity to punish effectively, everything else is kept constant across conditions. If punishment is indeed satisfactory in the IF condition, we expect that subjects are also willing to incur cost to punish the defector. In fact, those subjects who show the strongest activation of reward-related areas in the IF condition should also be those who incur the largest cost of punishing in the IC condition. Moreover, if subjects reasonably weigh the costs and the satisfaction of punishing B, that is, if they punish as long as the marginal costs are below the marginal "benefits" of punishing, punishment in the IC condition should also be experienced as satisfactory. Thus, we predict that reward-related areas will also be activated in the IC-IS condition.

If B keeps all the money in the NC condition, he is not responsible for this action because a random device forced him to do so. We therefore predict that A does not view B's act as unfair and has no desire, or a strongly reduced desire, to punish B. If there is no desire to punish, punishment is unlikely to yield satisfaction. For this reason, we predict activations in reward-related areas in the IF-NC and the IC-NC contrasts. Finally, we can also compute the combined contrast (IC + IF) – (IS + NC). We should also observe activations in reward-related areas in this contrast, because there is the desire and the opportunity to punish both in the IC and the IF conditions, whereas there is no opportunity for punishment in the IS condition and there is no desire to do so in the NC condition. If either the opportunity or the desire to

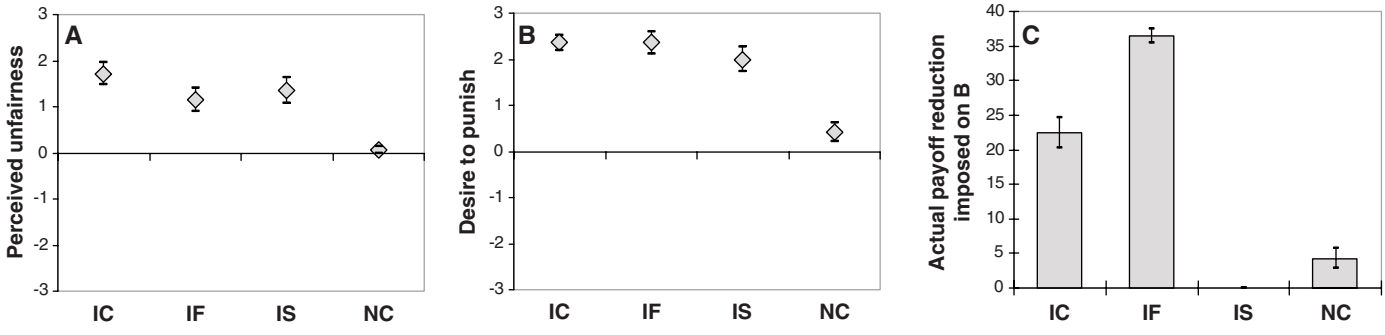

Fig. 1. Player A's feelings about player B and actual payoff reduction imposed on B. (**A**) Player A's perceived unfairness if B kept all the money. During the 10-min interval between PET scans, player A indicated on a seven-point Likert scale (from –3 to +3) whether he perceived B's action in the previous trial as fair or unfair. Maximal fairness is indicated by –3, maximal unfairness by +3. The figure shows the mean perception across subjects ± SE. (**B**) Player A's desire to punish B if the latter kept all the money. During the 10-min interval between PET scans, A indicated on a seven-point Likert scale (from –3 to +3) the strength of his desire to reward or to punish B. The maximal desire to reward is indicated by –3, the maximal desire to punish by +3. We show the mean desire to reward/punish ± SE. (**C**) Actual payoff reduction imposed on B if the latter keeps all the money. The figure shows the mean payoff reduction A imposed on B ± SE. In the IS condition, the economic payoff of B could not be reduced.

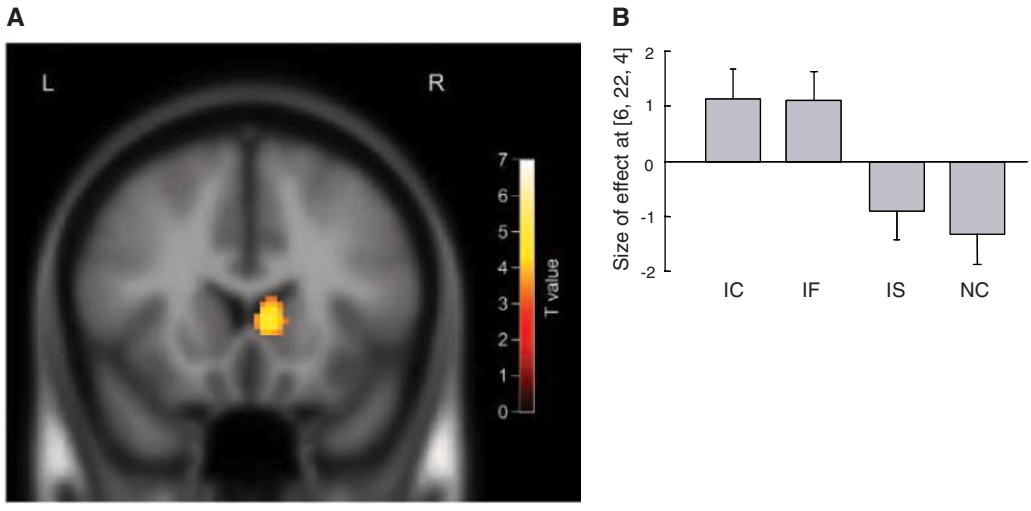

Fig. 2. (**A**) Activation in the caudate nucleus in conditions in which subjects indicated a strong desire to punish and could effectively do so (IC and IF) relative to conditions in which there is no effective punishment or the desire to punish is absent (IS and NC). (**B**) Effect sizes at the peak of blood-flow increase in the caudate nucleus. Bars indicate caudate activity in each condition relative to the mean brain activation ± SD.

punish effectively is absent, punishment can yield little or no satisfaction.

Questionnaire and behavioral results support these hypotheses (Fig. 1, A to C). Player A views B's act to keep all the money as very unfair in all three intentional conditions (IC, IF, and IS), whereas he views it as nearly neutral in the NC condition (Fig. 1A; sign test for equality of medians, $P < 0.002$ for all pair-wise comparisons of the NC condition with each intentional condition). Likewise, player A exhibits a strong desire to punish B in all three intentional conditions, but this desire is nearly absent in the NC condition (Fig. 1B; sign test for equality of medians, $P < 0.012$ for all pair-wise comparisons of the NC condition with each intentional condition). Moreover, player A imposes much higher payoff reductions on B in those conditions in which B intentionally abuses his trust, whereas almost no punishment is imposed on B in the NC condition (Fig. 1C; $P \leq 0.001$ for sign test comparing IC and NC and for the test comparing IF and NC). Twelve of 14 subjects punished B if he kept all the money in the IC condition, and all 14 subjects punished B in the IF condition. This contrasts with the NC condition, in which only 3 of 14 subjects reduced B's payoff, and those who did so punished only a little.

Does punishment activate reward-related brain circuits? Among the areas showing greater activation in the contrasts described above is the caudate nucleus (Table 1), which is activated in all five contrasts in which we predicted the activation of reward-related areas. For example, the peak activation in the contrast (IC + IF) – (IS + NC) is observed at the coordinates (6, 22, 4), the head of the caudate nucleus (Fig. 2A; $P < 0.05$, corrected for multiple comparisons). Moreover, effect-size analysis at the peak of the blood flow in the caudate (Fig. 2B) indicates that the different conditions contributed to this activation in the predicted way: We observe above-average activations in the IC and IF conditions, in which subjects express a strong desire to punish and can satisfy this desire; we observe below-average activations in the IS and NC conditions, in which subjects either cannot satisfy their desire to punish or feel no desire to punish. This pattern of caudate activation is also replicated in the individual contrasts IF-IS, IC-IS, IF-NC, and IC-NC (Table 1).

Table 1. PET results.

Contrast	Region (BA)	Coordinates			*Z* value
		x	*y*	*z*	
(IC + IF) – (IS + NC)	Caudate nucleus	6	22	4	5.11*
	Thalamus	22	–24	10	4.43*
IF-IS	Caudate nucleus	6	22	4	3.55
	Thalamus	22	–22	10	4.21
IC-IS	Caudate nucleus	6	24	2	3.70
	Thalamus	22	–22	10	4.15
IF-NC	Caudate nucleus	6	22	4	4.18
IC-NC	Caudate nucleus	6	22	4	4.23
IC-IF	Ventromedial prefrontal cortex (BA 10)	2	54	–4	4.59
	Medial orbitofrontal cortex (BA 11)	–4	52	–16	3.35

The table shows MNI coordinates (*x*, *y*, *z*) that locate the maxima of changes in blood flow. * indicates significant activations at the $P < 0.05$ level, corrected for multiple comparisons. Otherwise, the threshold for hypothesized brain regions is $P < 0.001$, uncorrected. For all activations at $P < 0.001$, see (*21*). BA denotes Brodmann area. IC is the intentional and costly condition, IF the intentional and free condition, IS the intentional and symbolic condition, and NC the nonintentional and costly condition. A negative value for the *x* coordinate indicates the left side of the brain. MNI denotes Montreal Neurological Institute.

The activation of the caudate in those conditions in which subjects expressed a strong desire to punish and could indeed punish is particularly interesting in light of this region's prominent role in the processing of rewards. In animals, this brain region has been associated with the processing of reward information by means of lesion experiments with rats (*24*) and single-cell recordings in nonhuman primates (*10*, *19*). Caudate activations in humans have been reported in several neuroimaging studies that investigated reward processing (*12*, *13*, *15*, *16*, *25*, *26*); in addition, caudate activations have been observed with reinforcers such as cocaine (*27*) and nicotine (*28*). Some neuroimaging studies even indicate that parametric increases in monetary rewards are positively correlated with caudate activations (*14*, *15*).

We also found increased blood flow in the thalamus (Table 1) in those conditions in which subjects expressed a strong desire to punish and could punish (IC and IF) relative to the symbolic punishment condition. No thalamus activation was found when IC and IF were compared with the NC condition, in which the desire to punish was absent. Activations in the thalamus have been reported in human neuroimaging studies investigating processing of monetary reward (*14*, *16*, *26*). Taken together, our findings suggest a prominent role of the caudate nucleus, with possible contributions of the thalamus, in processing rewards associated with the satisfaction of the desire to punish the intentional abuse of trust.

This result would be further supported if we were able to show that those subjects with a stronger caudate activation punish more strongly. We examined this question by computing

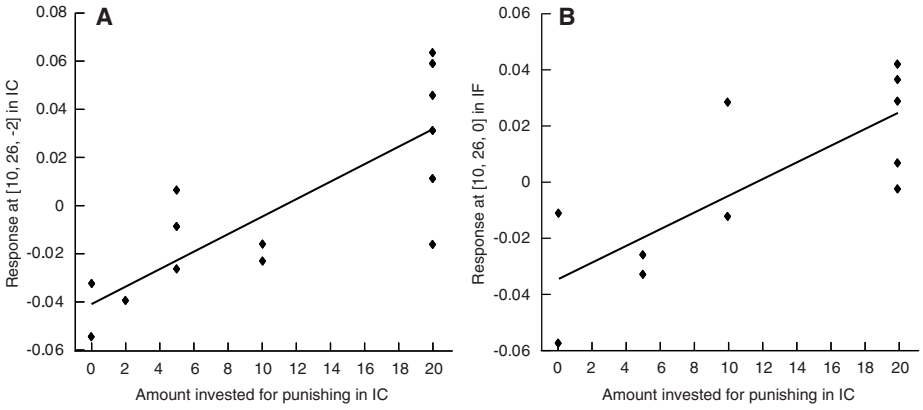

Fig. 3. (**A**) Positive correlation between caudate activation at coordinates [10, 26, –2] and the amount of money spent on punishment in the IC condition. Subjects with higher caudate activation in the IC condition spent more money on punishment in this condition. (**B**) Positive correlation between caudate activation at coordinates [10, 26, 0] in the IF condition in those subjects that punished maximally and the amount of money spent on punishment by these subjects in the IC condition. Subjects with higher caudate activation at the same (maximal) level of punishment in the IF condition spent more money on punishment in the IC condition.

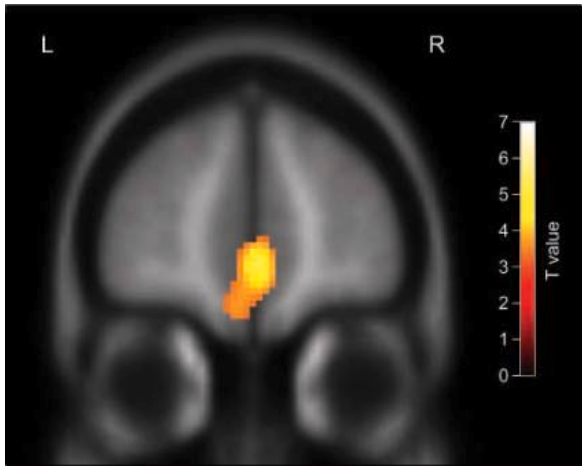

Fig. 4. The role of the prefrontal cortex in integrating the benefits and costs of punishing. Activation of the ventromedial prefrontal cortex and the medial orbitofrontal cortex in the condition where subjects have a strong desire to sanction but where sanctioning is costly for the punisher (IC) relative to the condition where there is also a strong desire to sanction but sanctioning is costless for the punisher (IF).

the correlation between brain activation and the actual monetary punishment across subjects in the IC condition. We did indeed find a positive correlation between caudate activation (at coordinate position [10, 26, –2]; $P < 0.001$) and investments in punishment (Fig. 3A). This correlation can be interpreted in two ways. One interpretation is that a higher punishment could have induced stronger feelings of satisfaction, which suggests that stronger punishment causes stronger caudate activation. Alternatively, subjects who expected higher satisfaction from punishing a defector could have been willing to invest more money in punishment. If the second interpretation is true, the causality is reversed: A higher caudate activation reflects the greater expected satisfaction from punishment, which, in turn, causes higher investments in punishment. The second interpretation is particularly interesting in light of the caudate's oft-noted role in the integration of reward information and behavioral information in the sense of a goal-directed mechanism (*9*).

Brain activations and the decision to punish. Our data enable us to discriminate between the two interpretations. The key is to examine the caudate activations of the 11 subjects in the IF condition who punished maximally. Because these subjects imposed the same punishment on B, differences in their caudate activations in the IF condition cannot be due to differences in punishment. However, if caudate activation reflects the expected satisfaction from a given level of punishment, the differences in caudate activations across these subjects may reflect differences in expected satisfaction from a given level of punishment. If this interpretation is true, we should observe that subjects who exhibit a higher caudate activation in the IF condition, that is, subjects who expect a higher satisfaction from the same level of punishment, are willing to invest more money in punishment if it is costly to punish. In other words, this interpretation predicts that among the subjects who punished maximally in the IF condition, those with higher caudate activation in the IF invest more in punishment in the IC condition. This prediction is supported by a positive correlation between caudate activation in the IF and the amount invested in punishing in the IC condition (Fig. 3B; $P < 0.002$). This finding lends support to the hypothesis that the observed activations in the dorsal striatum reflect expected satisfaction from punishment, which is consistent with the view of the dorsal striatum as a key area involved in goal-directed, rewarding behavior.

If the punishment of intentional defectors is rewarding, player A faces a trade-off in the IC condition but not in the IF condition, because punishment is costly in the former. Player A has to weigh the emotional satisfaction of punishing against the monetary cost of punishing, which requires integration of separate cognitive operations in the pursuit of a behavioral goal. Much evidence indicates that the prefrontal and the orbitofrontal cortex are involved in integrating separate cognitive operations and decision making (*29*–*32*). Our behavioral data suggest that in the IC condition subjects face a decision problem because most subjects punish maximally in the IF condition, whereas the cost for the punisher reduces punishment significantly in the IC condition (Fig. 1C; sign test, $P = 0.039$). Therefore, we expected activations in the pre- and orbitofrontal cortex in the IC-IF contrast. The data show (Table 1 and Fig. 4) that the ventromedial prefrontal (BA 10) and the medial orbitofrontal cortex (BA 11) are activated in this contrast. The activation of BA 10 is interesting because this area has been associated with the integration of two or more separate cognitive operations in the pursuit of higher behavioral goals (*33*). The activation in the medial orbitofrontal cortex is also interesting because of this region's oft-noted involvement in difficult choices that require the coding of reward value (*34*, *35*). These activations also provide indirect support for the hypothesis that punishing defectors involves satisfaction, because if that were not the case, no benefits would have to be weighed against the costs of punishing and no integration would have to take place.

These results also illustrate the stark contrast between the biological and the psychological definitions of altruism (*4*). According to the biological definition, an act is altruistic if it is costly for the actor and confers benefits on other individuals. It is completely irrelevant for this definition whether the act is motivated by the desire to confer benefits on others, because altruism is solely defined in terms of the consequences of behavior. This contrasts with the psychological definition, which also requires that the act be driven by an altruistic motive that is not based on hedonic rewards (*36*). Thus, the punishment of defectors is an altruistic act in the biological sense because, typically, it is costly for the punisher and induces the punished individual to defect less in future interactions with others. However, our results suggest that it is not an altruistic act in the psychological sense.

Conclusions. Our study is part of recent attempts in "neuroeconomics" and the "cognitive neuroscience of social behavior" to understand the social brain and the associated moral emotions (*37–44*). However, this study sought to identify the neural basis of the altruistic punishment of defectors. The ability to develop social norms that apply to large groups of genetically unrelated individuals and to enforce these norms through altruistic sanctions is one of the distinguishing characteristics of the human species. Altruistic punishment is probably a key element in explaining the unprecedented level of cooperation in human societies (*1–3*). We hypothesize that altruistic punishment provides relief or satisfaction to the punisher and activates, therefore, reward-related brain regions. Our design generates five contrasts in which this hypothesis can be tested, and the anterior dorsal striatum is activated in all five contrasts, which suggests that the caudate plays a decisive role in altruistic punishment. Caudate activation is particularly interesting because this brain region has been implicated in making decisions or taking actions that are motivated by anticipated rewards (*17–20*). The prominent role of the caudate in altruistic punishment is further supported by the fact that those subjects who exhibit stronger caudate activation spend more money on punishing defectors. Moreover, our results also shed light on the reasons behind this correlation. Subjects who exhibit higher caudate activation at the maximal level of punishment if punishment is costless for them also spend more resources on punishment if punishment becomes costly. Thus, high caudate activation seems to be responsible for a high willingness to punish, which suggests that caudate activation reflects the anticipated satisfaction from punishing defectors. Our results therefore support recently developed social preference models (*6–8*), which assume that people have a preference for punishing norm violations, and illuminate the proximate mechanism behind evolutionary models of altruistic punishment.

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22. To maintain symmetry with case 1, player B can also give half of his money to A if A does not trust him. However, because all subjects (except one) in the role of A trusted B, this contingency almost never occurred.
23. In all conditions, both players received an additional endowment of 20 MUs after player B made his decision. This endowment allowed A to finance the cost of punishment in those conditions in which punishment was also costly for him. If A did not punish, both players kept the 20 MUs. If punishment was not costly for A, he kept the 20 MUs regardless of the number of assigned punishment points.
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Supporting Online Material

www.sciencemag.org/cgi/content/full/305/5688/1254/DC1
Materials and Methods
Table S1
References

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Spatial Representation in the Entorhinal Cortex

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As the interface between hippocampus and neocortex, the entorhinal cortex is likely to play a pivotal role in memory. To determine how information is represented in this area, we measured spatial modulation of neural activity in layers of medial entorhinal cortex projecting to the hippocampus. Close to the postrhinal-entorhinal border, entorhinal neurons had stable and discrete multipeaked place fields, predicting the rat's location as accurately as place cells in the hippocampus. Precise positional modulation was not observed more ventromedially in the entorhinal cortex or upstream in the postrhinal cortex, suggesting that sensory input is transformed into durable allocentric spatial representations internally in the dorsocaudal medial entorhinal cortex.

An extensive body of evidence suggests that the hippocampus is essential for fast encoding and storage of new episodic memories but has a more limited role in remote memory, which is thought to be stored primarily in the neocortex (*1–4*). Memory consolidation in the neocortex appears to be a slow and gradual process based on repeated interactions with the hippocampus (*2*, *3*). These interactions must be mediated largely through the entorhinal cortex, which interconnects the hippocampus with nearly all other association cortices (*5–8*). Understanding how information is processed in the entorhinal cortex is thus essential to resolving the interaction between the hippocampus and neocortex during encoding, consolidation, storage, and retrieval of memory.

However, little is known about how sensory input is represented in the entorhinal cortex. Although hippocampal memories are expressed at the neuronal level as representations with evident correlates to the spatial and nonspatial structure of the external environment (*6*, *9*, *10*), the functional correlates of entorhinal neurons

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are less manifest. Recordings from parahippocampal areas that provide input to the hippocampus suggest that neurons in these regions are only weakly modulated by the position of the animal (*11*–*15*). The contrast between the weak spatial input signal and the strong spatial output signal from the hippocampus has been taken as evidence for intrahippocampal computation of allocentric location (*11*, *12*) and a fundamental involvement of the hippocampus in spatial navigation (*9*).

The attribution of spatial algorithms to the hippocampus rests on the assumption that the upstream parahippocampal cortices have been adequately sampled. The parahippocampal cortex comprises a number of subregions with topographically organized internal and external connections, suggesting a modular organization (*7*, *8*, *16*, *17*). The entorhinal cortex, for example, segregates into overlapping recurrently connected bands parallel to the rhinal sulcus that cut across the medial and lateral subdivisions of the area (*7*, *16, 17*) (Fig. 1A). The most dorsolateral band provides the strongest input to the dorsal part of the hippocampus (*7*, *16*), which has the sharpest and most information-rich place fields (*18*) and plays a more essential role in spatial learning than the ventral hippocampus (*19*, *20*). This dorsolateral band also receives most of the visuospatial input to the entorhinal cortex (*8*). Yet none of the previous recordings suggesting weak spatial modulation in entorhinal cortex were made in this dorsolateral band (*11*–*13*). Thus, we reexamined spatial representation upstream of the hippocampus by recording along the entire dorsolateral-to-ventromedial axis of the medial entorhinal cortex (MEC) (*21*).

Topographical organization of entorhinal-hippocampal connections. We first labeled the projections to the hippocampus that arise in the dorsolateral band portion of MEC with the use of the anterogradely transported tracer biotinylated dextrane amine (BDA) (Fig. 1B). Likewise, we visualized the projections originating from the ventromedial band portion of MEC in the same sagittal plane (Fig. 1C). All dorsolateral injections ($n = 3$) resulted in strong anterograde labeling exclusively in the dorsal hippocampus, with labeling limited to well-defined portions of the molecular layer of the dentate gyrus and subiculum, and stratum lacunosum-moleculare of CA3 and CA1 (Fig. 1B; supporting online text). Injections in the ventromedial band portion of MEC ($n = 3$) produced labeling exclusively in the ventral hippocampus but with a comparable distribution in layers and fields (Fig. 1C). These observations indicate topographically organized projections from MEC to the hippocampus with a dorsolateral-to-ventromedial axis of origin in MEC corresponding to the dorsal-to-ventral axis of the hippocampus (*16*, *22*).

Heterogeneity of spatial firing in entorhinal cortex. A total of 220 putative excitatory cells in layers II and III were recorded from 14 rats with electrodes in the dorsolateral ($n = 10$; Figs. 1A and 2A), intermediate ($n = 1$; Figs. 1A and 3A), or ventromedial ($n = 3$; Figs. 1A and 3C) bands of MEC, with the dorsolateral and ventromedial recording locations matching the tracer injection sites. Spike activity was recorded while rats collected food in a square enclosure (*21*). In the dorsolateral band, putative excitatory cells had sharp and coherent place fields in the test box (Figs. 2B and 4; $n = 135$). Nearly all cells had multiple firing fields (with a median number of 4; Fig. 4E), but individual fields were clearly delimited against the intervening background. Firing was only weakly modulated by the rat's direction of movement (Figs. 2C and 4K). The multiple firing fields of a cell showed a remarkably dispersed distribution compared to a shuffled distribution (Fig. 2D). The distance between neighboring fields was larger than expected from a uniform random distribution (Wilcoxon signed-ranks test: $Z = 9.0$, $P < 0.001$), and the range was narrower ($Z = 5.6$, $P < 0.001$). The location of the fields was generally consistent across trials and days (Figs. 2B and 4J; fig. S1). The number of subfields was unrelated to the confidence with which the unit could be separated from other units recorded on the same tetrode (figs. S2 and S3).

We compared place fields of these dorsolateral cells with those of cells in intermediate ($n =$

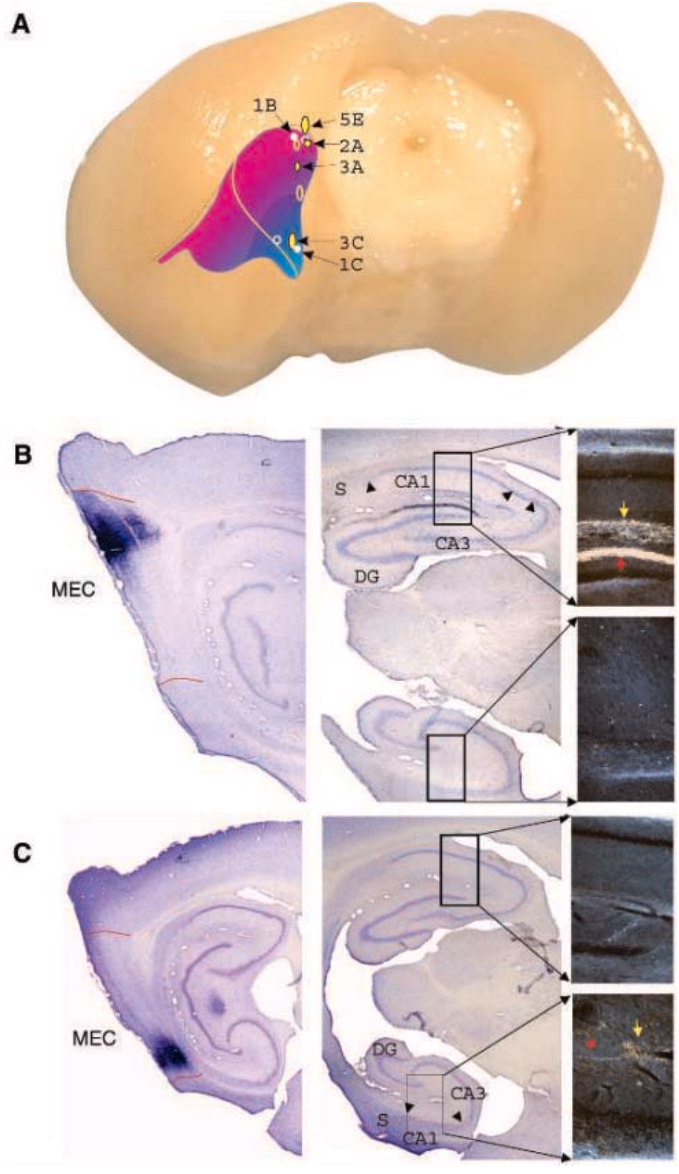

Fig. 1. Topographic projections from MEC to hippocampus. (**A**) Ventral-posterior view of a whole rat brain showing the outline of the left entorhinal cortex (colored surface) and the rhinal fissure (stippled gray line). The dorsolateral-to-ventromedial gradient of entorhinal extrinsic connectivity (magenta-to-blue) cuts across both lateral and medial entorhinal subdivisions (border indicated by yellow line). Filled white markers indicate sites of tracer injection in (B) and (C). Open white markers indicate injections not illustrated. Filled yellow markers show recording positions in Figs. 2A, 3A, 3C, and 5E. Open yellow markers indicate selected additional recording positions in MEC. (**B**) Sagittal sections illustrating the projections from the dorsolateral-band zone of MEC to the hippocampus. (Left) Injection site of BDA. Dorsal and ventral borders of MEC are indicated by red lines. (Middle) Low-power brightfield sagittal section showing dense staining in dorsal but not ventral hippocampus (black arrowheads indicate borders between hippocampal subfields). (Right) High-power darkfield photomicrographs of indicated areas in the dorsal and ventral hippocampus. (Top right) Bright orange band corresponds to dense labeling in the middle molecular layer of the dentate gyrus (red arrow) (*21*). The labeling more dorsally (yellow arrow) corresponds to the less massive termination of MEC fibers in the proximal half of CA1. (**C**) Projections from the ventromedial region of MEC. Note the absence of staining in dorsal hippocampus (darkfield picture, top right) and moderate labeling in fields CA1 and dentate gyrus of the ventral hippocampus (darkfield picture, bottom right; yellow and red arrows, respectively) (*21*).

22) and ventromedial ($n = 63$) parts of MEC. At intermediate positions, most cells were spatially modulated, but their fields were broader and less coherent and lacked the characteristic intervening silent areas of the multipeaked fields in the dorsolateral band (median number of fields: 1.75; Figs. 3B and 4). At the most ventromedial positions, only very weak spatial modulation was apparent (Figs. 3D and 4), even in cells classified as clearly separated from their peers (fig. S2C).

Quantitative analyses confirmed that the neuronal response to location differed along the dorsolateral-to-ventromedial axis of MEC. The spatial information rate in bits/s of all cells recorded in MEC correlated significantly with the position of the recording electrode along the dorsolateral-to-ventromedial axis ($r = 0.78$; $n = 14$ rats; $P = 0.001$). Information rates in the dorsolateral, intermediate, and ventromedial bands were strikingly different, with a significantly larger proportion of high–information rate cells in the dorsolateral band [Fig. 4I; Kruskal-Wallis test: $\chi^2(2) = 111.1$, $P < 0.001$; supporting online text]. Cells in the dorsolateral band had a larger number of nonoverlapping firing fields per cell [Fig. 4E; $\chi^2(2) = 103.8$; $P < 0.001$]. These fields were smaller [Fig. 4F; $\chi^2(2) = 31.9$, $P < 0.001$] and more coherent [Fig. 4H; $\chi^2(2) = 117.5$, $P < 0.001$] than in the intermediate and ventromedial band, and the peak rates were higher [Fig. 4D; $\chi^2(2) = 81.2$; $P < 0.001$]. The collective activity of a small number of simultaneously recorded dorsolateral cells was sufficient to reconstruct accurately the trajectory of the rat (*23*) (movie S1). The fields were correlated across trials at all dorsolateral-to-ventromedial levels, but the stability was higher in the dorsolateral band [Fig. 4J; $\chi^2(2) = 27.7$, $P < 0.001$]. Modulation by the rat's direction of movement was weak in all regions (Fig. 4K; $\chi^2 = 0.3$; not significant).

Comparison with target areas in the hippocampus. The positional firing properties of the superficial dorsolateral band neurons suggest that spatial location is expressed accurately before signals enter the hippocampus. We compared directly the firing fields of cells in the dorsolateral band of MEC (10 rats) with those of simultaneously recorded cells in the connectionally related portion of dorsal CA 1 (3 rats; 56 cells) (Figs. 1B and 4). Sharply defined place fields predominated in both cell groups. The average information rate in bits/s was not different (Wilcoxon rank-sum test: $Z = 1.47$; $n = 114$), nor was the spatial coherence of the firing ($Z = 1.44$). However, the number of subfields per cell was larger in MEC than in CA1 ($Z = 2.75$, $P < 0.01$), the subfields were slightly smaller ($Z = 1.96$, $P = 0.05$), and the peak rate was higher ($Z = 2.80$, $P < 0.005$). Modulation by direction of movement was lower in MEC than in CA1 ($Z = 4.23$, $P < 0.001$). Firing rate maps were stable between trials in both areas, but were less in MEC than in CA1 ($Z = 3.73$, $P < 0.001$; Fig. 4 and fig. S1B).

Spatial firing fields after removal of hippocampal output. Output from the hippocampus to deep layers of MEC may influence neuronal firing in superficial layers (*7*, *17*, *24*). The precise spatial firing of layer II and III neurons in the dorsocaudal MEC may therefore be influenced by operations taking place within the hippocampus. We examined the spatial firing of 30 MEC neurons in five postoperatively trained rats with selective bilateral hippocampal lesions. In four rats, the lesions were complete throughout the dorsal 80 to 100% of the hippocampus (Fig. 5A). The fifth rat had a complete lesion of CA3 and CA1 (Fig. 5C). All five rats had cells with discrete multipeaked place fields in layer II of the dorsolateral band (Fig. 5, B and D). The lesions had no significant effect on the spatial information rate (lesioned rats: 0.62; control rats: 0.72; $Z = 1.53$), the median number of peaks (3.5 versus 4; $Z = 1.07$), or the mean field size (0.19 m^2 versus 0.13 m^2; $Z = 1.38$) (compare with Fig. 4, A and B). However, they decreased the spatial coherence (0.47 versus 0.70; $Z = 5.2$, $P < 0.001$) and the dispersedness of the firing

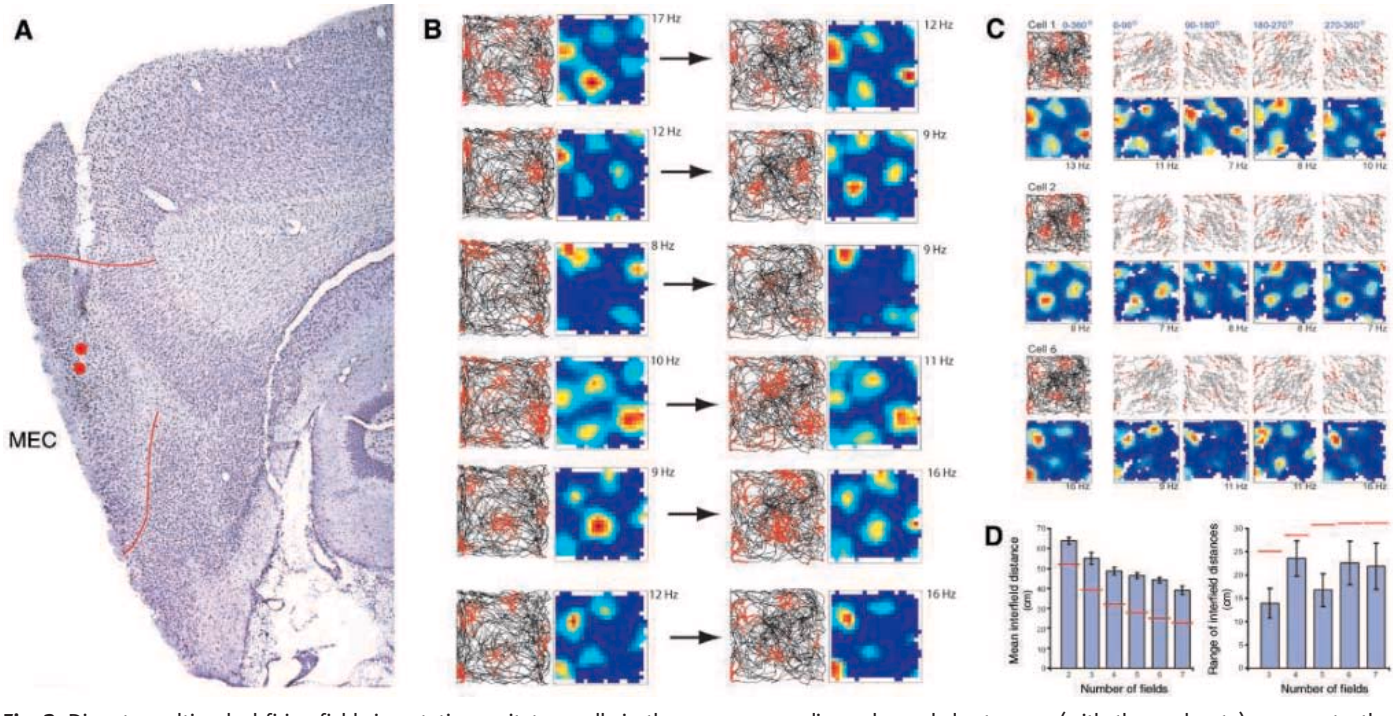

Fig. 2. Discrete multipeaked firing fields in putative excitatory cells in the dorsolateral band of MEC. (**A**) Nissl stain showing electrode locations in layers III (upper red circle) and II (lower red circle) of the dorsolateral band (sagittal section; see also Fig. 1A). Red lines indicate borders of MEC toward postrhinal cortex (dorsal) and parasubiculum (ventral). (**B**) Firing fields of simultaneously recorded cells from the lower location in (A). Each row shows one cell, and each pair of columns one trial. The trajectory with superimposed spikes (red) is shown to the left in each pair of columns; the corresponding color-coded rate map (with the peak rate) appears to the right. The color scale is linear with blue as zero and red as maximum. Regions not covered by the rat are in white. Note the multiple discrete firing fields that were stable across trials. (**C**) Trajectory maps and color-coded maps showing similar fields for each directional quadrant of body movement for three of the cells in (B). (**D**) Distance between neigboring firing fields in dorsolateral-band cells with more than two fields (all rats; mean, SEM, and range for each cell). Red lines indicate chance level.

fields (distance between neighboring fields: 39.8 cm versus 49.5 cm; $Z = 3.7$, $P < 0.001$), although the fields were still more dispersed than expected from a uniform random distribution (39.8 cm versus 32.2 cm; $Z = 4.1$, $P < 0.001$). The firing also became more dependent on the direction of movement (directionality index: 0.49 versus 0.21; $Z = 5.3$, $P < 0.001$), and the spatial correlation between trials declined (0.37 versus 0.70; $Z = 1.86$, $P < 0.05$, one-tailed Wilcoxon test).

Absence of discrete firing fields further upstream. To determine whether precise spatial information arises in MEC or is relayed from other areas, we recorded activity from the connectionally related parts of layers III and V of the postrhinal cortex, which represent the major source of visuospatial input to the dorsolateral band of MEC (*8*). Spikes were recorded from 48 well-isolated cells with broad waveforms in three rats (Fig. 5, E to G). The firing fields generally covered the entire recording environment (median field size: 0.55 m^2). Information rates were low (median 0.18 bits/s), as was the average stability of the spatial firing across trials (median correlation 0.25). No difference was observed between layers III and V. In one rat, the electrodes were turned into the dorsolateral band of MEC subsequent to postrhinal cortex (Fig. 5E). Sharp, multipeaked firing fields appeared as soon as the electrodes moved into entorhinal cortex (Fig. 5H).

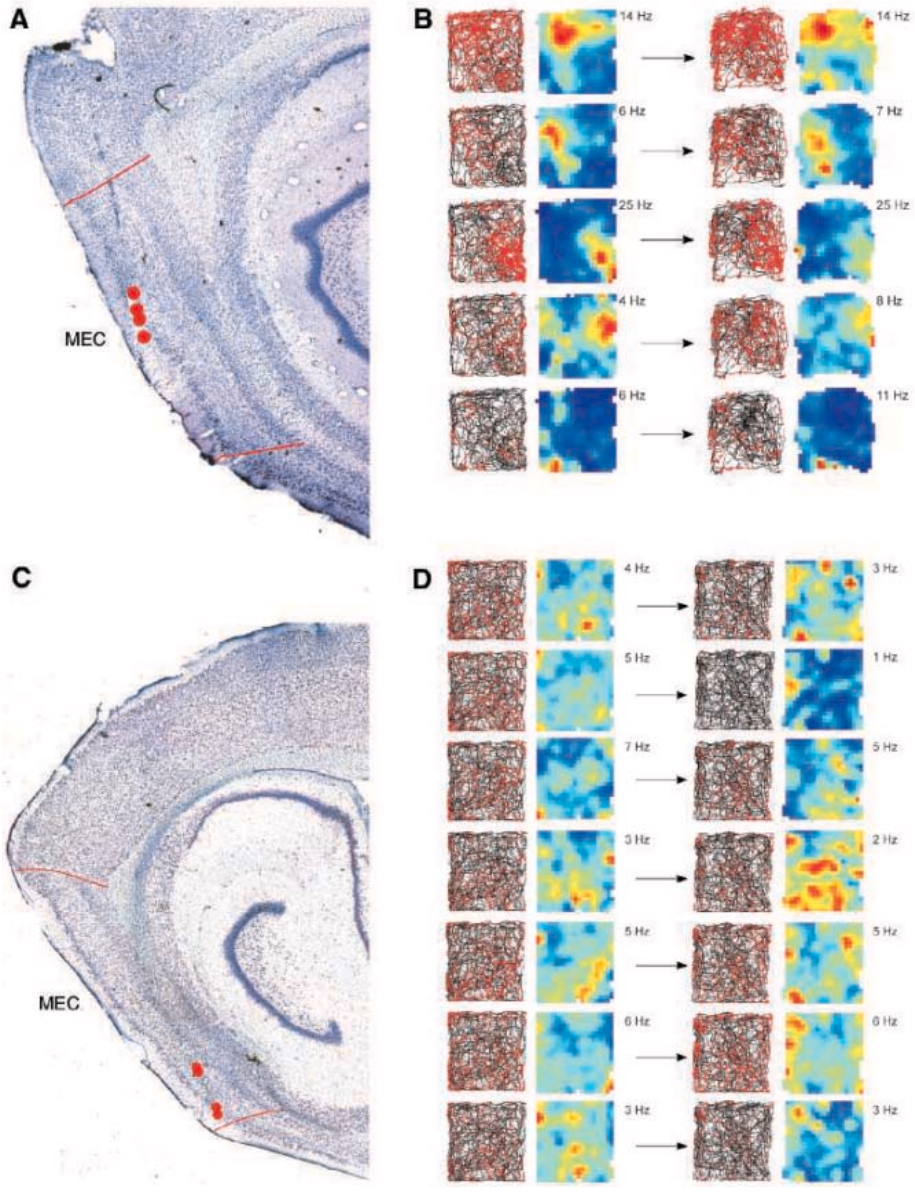

Fig. 3. Weak spatial modulation in the intermediate band (**A**) and absence of spatial modulation in the ventromedial band (**C**) of MEC. Sagittal sections indicating recording locations of layer II in the intermediate band [red circles in (A)] and in layers III and II of the ventromedial band [upper and lower red circles in (C), respectively] (see also Fig. 1A). Borders of MEC are indicated by red lines. (**B** and **D**) Firing fields of simultaneously recorded cells in layer II of the intermediate or ventromedial band [(B) and (D), respectively].

Discussion. Our data provide functional evidence for a modular organization of MEC (*7*, *8*, *16*, *17*). Allocentric view–independent spatial information is expressed primarily by neurons close to the border with the postrhinal cortex. This part of MEC is the predominant recipient of visuospatial information from the visual and parietal cortices (*8*). At more intermediate regions, firing fields get more dispersed, as reported previously (*11*–*13*). The near absence of position-modulated neurons in the most ventromedial region is consistent with the preponderantly nonspatial input to this area (*7*, *8*). The differences in spatial firing within MEC provide a rationale for the dominant involvement of the dorsal part of the hippocampus in spatial memory (*19*, *20*).

The fact that information about the rat's current location was expressed as strongly in superficial layers of the dorsocaudal MEC as in the hippocampus suggests that major steps in the computation of allocentric space occur upstream of the hippocampus (*25*). Although a single multipeaked entorhinal place field provides little information about the animal's location, the sharp and consistent delineation of individual peaks from the background permits the current position of the animal to be represented accurately by the collective firing of only a small number of superficial MEC neurons (*23*, *26*). Hippocampal return projections were not required to maintain the information-rich multipeaked firing pattern, but reverberation through the hippocampus appeared to strengthen the separation and directional independence of the firing fields (*27*).

Spatial information in the dorsocaudal MEC may be derived from afferent cell populations such as the postrhinal cortex and the dorsal presubiculum, which project heavily to superficial layers of the dorsolateral band of MEC (*8*, *28*). However, spatial modulation in the postrhinal cortex was weak and unstable (*15*). A similar insensitivity to allocentric location has been noted in the dorsal presubiculum, in which neurons are strongly modulated by head direction (*29*), and in areas with less extensive projections to the dorsolateral band of MEC (*14*, *30*). These observations suggest that spatial signals are actively transformed into cohesive allocentric representations within the entorhinal cortex itself. This transformation may also calibrate positional information with head-direction input from the dorsal presubiculum. Inputs from the dorsal presubiculum target a substantial proportion of excitatory neurons in the superficial layers of the dorsolateral band of MEC (*28*). Lesions of the dorsal presubiculum impair the directional control of polarizing stimuli on hippocampal place cells (*31*), implying that the dorsal hippocampus receives a conjunction of positional and directional input from MEC.

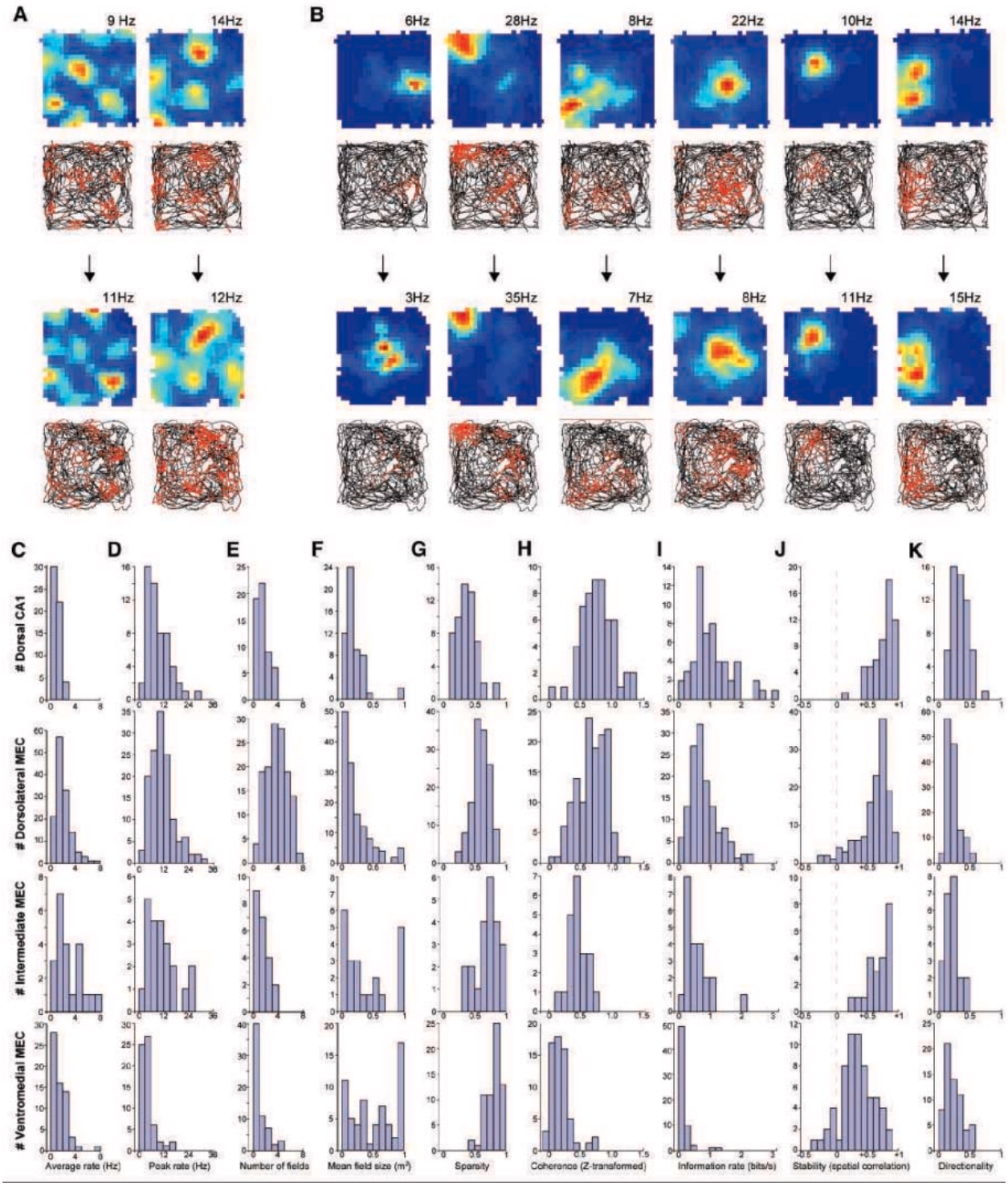

Fig. 4. Spatial modulation in superficial layers of MEC compared to hippocampal area CA1. (**A** and **B**) Color-coded rate maps and trajectory maps for cells recorded simultaneously from layer II in the dorsolateral band (A) and dorsal CA1 of the contralateral hippocampus (B). Each column shows one cell. The top two rows show trial 1; the bottom two rows show trial 2. (**C** to **K**) Quantitative analysis of spatial modulation in putative excitatory cells of layers II and III in dorsolateral, intermediate, and ventromedial bands of MEC as compared to pyramidal cells in dorsal CA1 (all cells in all regions). Panels show distribution of average rate (C), peak rate (D), number of fields (E), mean field size (F), sparsity (G), spatial coherence (H), spatial information rate (I), stability (J), and modulation by movement direction (K) (*21*, *23*).

Although our data show that the animal's current location is represented accurately upstream of the hippocampus, there were several noticeable differences between the spatial codes in MEC and hippocampus. First, place fields were slightly more stable across trials in the hippocampus. Although some cells fired repeatedly at exactly the same locations in both areas, new or dislocated fields were more common in MEC, pointing to a stronger involvement of the hippocampus in storage or retrieval of the afferent information. Unlike the MEC, the hippocampus may store information in such a manner that the same representation can be retrieved even with slight fluctuation of the retrieval cues across

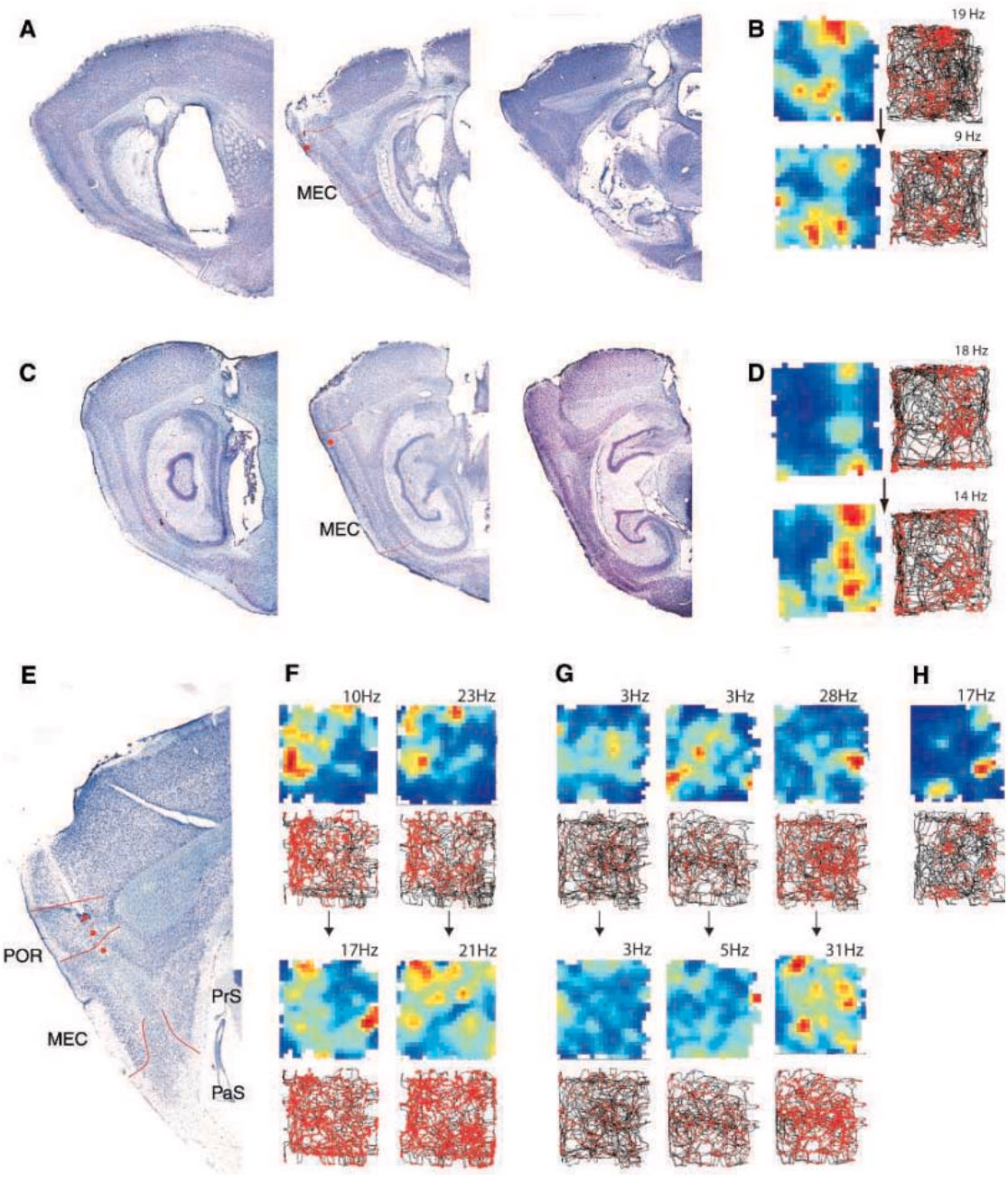

Fig. 5. Spatial firing in the dorsolateral band may reflect intrinsic computations of the MEC. (**A** to **D**) Spatial modulation in the dorsolateral band of MEC in two rats with ibotenate lesions of the hippocampus (three sagittal levels from lateral to medial). The rat in (A) and (B) had a complete lesion of CA3, CA1, dentate gyrus, and subiculum; the one in (C) and (D) had a complete lesion of CA3 and CA1, but dentate gyrus and subiculum were partly spared. Red circles indicate electrode locations in layer II; red lines indicate borders of MEC. Both animals had cells with discrete multipeaked firing fields, but the coherence of the fields was reduced. (**E** to **H**) Absence of strong spatial modulation upstream in adjacent postrhinal cortex. (E) Sagittal section through the postrhinal cortex (POR) and MEC indicating recording locations (red circles) and regional borders (parasubiculum, PaS; presubiculum, PrS; see also Fig. 1A). Note that two recording locations were in POR (layers V and III) and one in MEC (layer III). (F and G) Dispersed and unstable firing fields of postrhinal broad-waveform cells at the upper (F) and lower (G) recording position in POR. (H) Multiple discrete firing fields in a layer-III neuron at the succeeding recording position in MEC.

trials (pattern completion) (*32*–*35*). Second, firing fields in MEC were less influenced by the rat's direction of movement in a two-dimensional environment. Directional modulation in the hippocampus may arise as part of a hippocampal orthogonalization process in which incoming patterns are disambiguated from related but nonidentical patterns already stored in the network (*32*, *33*, *36*, *37*). This process may include the separation of trajectories that run through the same location but belong to different behavioral sequences (*13*, *38*–*40*). A hippocampal involvement in this process is consistent with the larger proportion of cells with trajectory-specific firing in deep entorhinal layers (downstream of the hippocampus) than in superficial layers (upstream of the hippocampus) (*13*). Third, the spatial structure of firing was different in dorsocaudal MEC and hippocampus. How discrete and regularly spaced firing fields arise in MEC and how they transform into single-peaked representations in the hippocampus remain unresolved issues. The transformation appears to be more pronounced in the hippocampus than in the dentate gyrus, where place cells often have multiple fields (*41*).

Although the differences in stabilization and directional modulation were small, they may become more pronounced in tasks that challenge memory retrieval. The similarities in spatial coherence and information rate and the differences in stabilization and directional modulation suggest that the well-established role of the hippocampus in spatial navigation may reflect the essential nature of spatial input as an element of most episodic memories rather than a specific role in computing the animal's location within a given context. Rather than calculating location per se, hippocampal networks may transform spatial and nonspatial sensory signals into distinguishable representations that can be retrieved despite noisy changes in background context.

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Supporting Online Material
www.sciencemag.org/cgi/content/full/305/5688/1258/DC1
Materials and Methods
SOM Text
Figs. S1 to S3
Movie S1

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REPORTS

Search for Low-Mass Exoplanets by Gravitational Microlensing at High Magnification

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Observations of the gravitational microlensing event MOA 2003-BLG-32/OGLE 2003-BLG-219 are presented, for which the peak magnification was over 500, the highest yet reported. Continuous observations around the peak enabled a sensitive search for planets orbiting the lens star. No planets were detected. Planets 1.3 times heavier than Earth were excluded from more than 50% of the projected annular region from approximately 2.3 to 3.6 astronomical units surrounding the lens star, Uranus-mass planets were excluded from 0.9 to 8.7 astronomical units, and planets 1.3 times heavier than Saturn were excluded from 0.2 to 60 astronomical units. These are the largest regions of sensitivity yet achieved in searches for extrasolar planets orbiting any star.

Gravitational microlensing events of high magnification occur when the foreground lens system comes into near-perfect alignment with the background source star. Suitable alignments are most readily found in the dense stellar fields in the Galactic bulge, where magnifications as high as 1000 are possible (*1*). In these events, the two images of the source star produced by the lens star merge to form a near-annular single-ring image. The events provide enhanced sensitivity for detecting planetary companions of the lens star because they can, depending on the planetary mass and position, perturb the ring-like image of the source star at times near the peak amplification (*1*–*5*). They complement events of low magnification that also provide substantial sensitivity for detecting extrasolar planets when "caustic crossings" occur (*6*–*9*). For both detection methods, the sensitivity to low-mass planets is enhanced in events with small (that is, main-sequence) source stars (*2*, *5*, *8*).

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High-magnification events can be detected in microlensing surveys that are sensitive to unresolved main-sequence stars and employ frequent sampling of target fields (*10*). However, most events occur on very faint sources and, although spectacular, are effectively very short-lived. Here we report observations of the very-high-magnification microlensing event MOA 2003-BLG-32/OGLE 2003-BLG-219 (hereinafter M32/O219). It was the first high-magnification event (with a nonbinary lens star) for which the full width at half maximum (FWHM) of the peak was intensively monitored. The observations were carried out with the 0.6-m telescope operated by the Microlensing Observations in Astrophysics (MOA) collaboration at the Mt. John Observatory in New Zealand, the 1.0-m telescope of the Wise observatory in Israel, and the 1.3-m Warsaw telescope operated by the Optical Gravitational Lensing Experiment (OGLE) collaboration at the Las Campanas Observatory in Chile.

M32/O219 was found independently by the MOA and OGLE microlensing surveys (*11*, *12*). The event brightened rapidly in the MOA survey on 12 June 2003 at α = 18h:05m:34s.64 and δ = –29°:06′:53″.6 (J2000.0); that is, at Galactic coordinates l = 2.04° and b = –3.86°. Intensive observations were carried out by MOA and subsequently by the Wise observatory during daylight hours in New Zealand. Unfortunately, the OGLE telescope was clouded out at the time, but constraining observations were made before the event peaked, and further constraining observations were made as it faded. The total data set presented here includes 44 Wise I-band images, 2 Wise V-band images, 921 MOA images taken from 2000 to 2003 in a wide red band, and 182 OGLE I-band images from 2001–2003. Except for the Wise V-band images, all images were analyzed using the difference-imaging technique to achieve the best possible photometric accuracy (*13*). This resulted in three independent sets of uncalibrated "delta-flux" measurements (tables S1 to S3).

The delta-flux measurements are well fitted by the theoretical light curve for microlensing of a point source by a single lens (Fig. 1). The light curve may be characterized by the normal parameters for gravitational microlensing. These are the Einstein radius crossing time t_E, the impact parameter u_0 of the source star trajectory with respect to the lens star in units of the Einstein radius r_E, and the time t_0 of closest approach of the source star to the lens star. The fitted values are $u_0 = 0.00191 \pm 0.00028$, t_0 = HJD2452803.4856 ± 0.0001, and $t_E = (20.87 \pm 0.11 \text{ days}) \times (0.00191/u_0)$ (*14*). The χ^2 for the best fit has χ^2/(degrees of freedom) = 1146.6/1129. The peak amplification A_{max} was 520 ± 80. Deviations of the light curve from that of a point source were searched for, but none were found. A 2σ upper limit of ~0.0016 for the ratio $r_s/r_{E'}$ was obtained, where r_s denotes the radius of the source star and $r_{E'}$ the Einstein radius projected to the plane of the source star.

The Wise images of the event were calibrated using the OGLE catalog of bulge stars (*15*) and the DoPHOT photometry program (*16*) for crowded fields (table S4). This yielded model-independent values of the peak magnitude of the event $I_{peak} = 14.251 \pm 0.018$, and of the color index of the source star $V - I = 1.51 \pm 0.03$. Here the smallness of the uncertainties results from the high magnification of the event. The microlensing fit yielded the baseline magnitude of the source star $I = 21.05 \pm 0.15$. This enabled the source star to be placed on a color-magnitude diagram of a nearby field (Baade's window) that was obtained by the Hubble Space Telescope (HST) (*17*). When allowance was made for the slightly different extinctions toward Baade's window and M32/O219, the source star for M32/O219 was found to lie on the perimeter of the HST diagram that corresponds to a metal-poor G-type main-sequence star with radius ~0.7 of the solar radius ($R_\odot$) located at the back of the Galactic bulge (fig. S1). The low metallicity of the source star was not anticipated, but we note that a similar result was reported recently for another event with a faint source star at the back of the Galactic bulge (*18*).

The sensitivity of high-magnification microlensing events to the presence of extrasolar planets depends not only on the peak magnification but also on the size of the source star, with smaller source stars providing higher sensitivity (*2*, *5*, *10*). The source size enters through the ratio $r_s/r_{E'}$, which, as noted above, is restricted by the light curve of M32/O219 to values <0.0016. For a lens of mass ~0.4 solar mass [typical for events with t_E ~ 20 days (*19*)] located near the back of the bulge, $r_s/r_{E'} \sim 0.0015$. For a lens of the same mass but located toward the front of the bulge, $r_s/r_{E'} \sim 0.0007$. The latter location is more likely, because it doubles the projected Einstein radius and the probability for lensing and is entirely consistent with the absence of source-size effects in the light curve. In what follows, we report the sensitivity of M32/O219 to planets for $r_s/r_{E'}$ equal to both 0.0007 and 0.0015. Values lower than 0.0007 are also possible, but they correspond to less likely masses and/or locations of the lens star.

We note that $r_E \approx 2.9$ astronomical units (AU) if $r_s/r_{E'} = 0.0007$. We also note that all the parameters in microlensing events, including $r_s/r_{E'}$, may be measured by observing the lens and the source as they diverge from one another after microlensing ceases (*20*), and that Monte Carlo simulations may also be carried out to constrain these parameters (*18*). Post-event observations would be especially valuable for events in which planets are detected.

Because the light curve of M32/O219 (Fig. 1) is consistent with that of a single lens, we used the data to determine exclusion zones for extrasolar planets orbiting the lens. Light curves were computed corresponding to the lens star, with trial planets placed at various positions and with various masses, and were compared to the observed data. The projected coordinates of the planet in the lens plane, x_p and y_p, were both allowed to range from $-8r_E$ to $+8r_E$ in steps of $r_E/32$ for planet:star mass ratio values $q = 10^{-6}$ and 10^{-5}, and from $-64r_E$ to $+64r_E$ in steps of $r_E/4$ for $q = 10^{-4}$ and 10^{-3}. In a previous search for extrasolar planets by microlensing, a finer grid was used (*21*).

A numerical light curve for each trial planet was generated using an inverse ray-shooting algorithm (*5*), and the χ^2 value with respect to the observed data was calculated. The value of χ^2 for the best-fit curve without an extrasolar planet was subtracted to provide a difference of chi-squares, $\Delta\chi^2$, for each trial. A threshold value of the difference was set at $\Delta\chi^2 = 40$ as the minimum required to exclude the presence of an extrasolar planet. This is smaller than the threshold value used in (*21*). However, in the previous

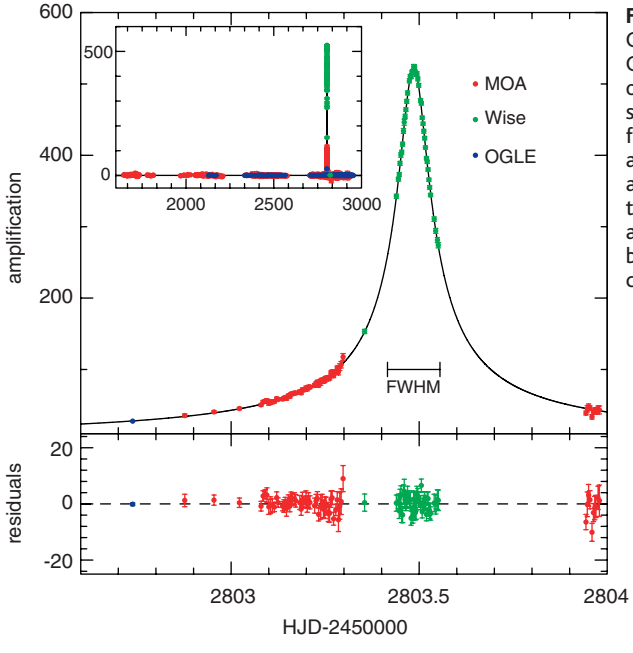

Fig. 1. Light curve of M32/O219 obtained by MOA (red), OGLE (blue), and Wise (green) over 1.5 days and 4 years (inset). The delta fluxes obtained from the difference imaging analysis were normalized to amplifications that correspond to the best fit for a single lens and a point source, as shown by the solid line. HJD is heliocentric Julian day.

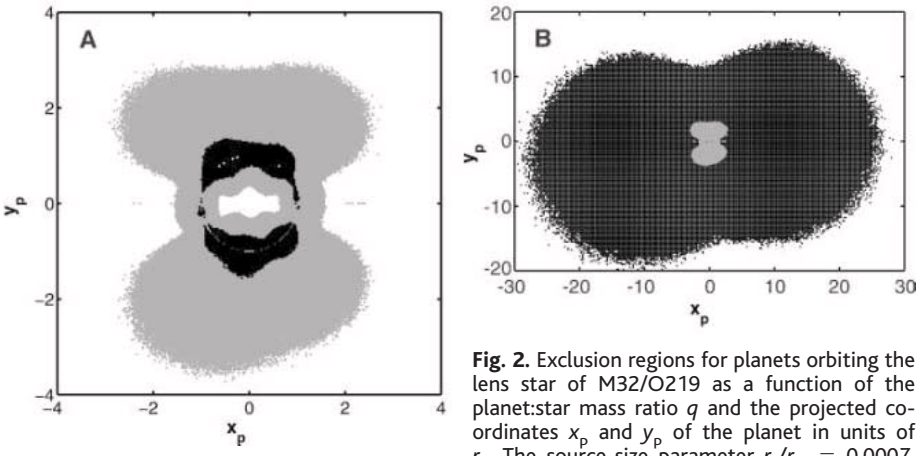

Fig. 2. Exclusion regions for planets orbiting the lens star of M32/O219 as a function of the planet:star mass ratio q and the projected coordinates x_p and y_p of the planet in units of r_E. The source-size parameter $r_s/r_{E'} = 0.0007$. (**A**) shows exclusion regions for low-mass planets with $q = 10^{-6}$ (white, close to the Einstein ring, upper hemisphere only), 10^{-5} (black), and 10^{-4} (gray), respectively, and (**B**) shows exclusion regions for $q = 10^{-4}$ (gray) and 10^{-3} (black). The sizes of the exclusion regions do not depend critically on the peak magnification. The regions for the magnification at its 1σ upper or lower limits would not be dissimilar (*18*). Indeed, doubling or halving the magnification does not dramatically alter the exclusion regions in these events (*10*). The orientation of the plots is similar to that used in (*5*), with the source star moving horizontally from left to right, just beneath the lens star.

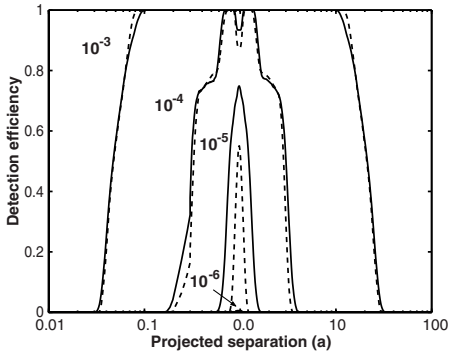

Fig. 3. Detection efficiencies for planets orbiting the lens star of M32/O219 as a function of the planet:star mass ratio q and the projected separation a in units of r_E. The q values range from 10^{-3} to 10^{-6}. The solid lines denote efficiencies for the source-size parameter $r_s/r_{E'} = 0.0007$, and the dashed lines denote efficiencies for the (less likely) value of 0.0015. These results demonstrate the gradual loss of sensitivity that occurs for low-mass planets as $r_s/r_{E'}$ increases. The results also illustrate a well-known degeneracy of the microlensing technique at high magnification. Planets at projected separations a and a^{-1} produce identical perturbations to the microlensing light curve (*2*). Information from space-based searches for extrasolar planets using the transit technique, which will provide statistics on the abundances of all types of planets at orbital separations <1 AU, could help to break this degeneracy. We note that the caustic-crossing technique (*6*–*9*) is not subject to the above degeneracy.

search, extrasolar planets were sought in events of lower magnification, where it is known that planetary perturbations may occur anywhere on the light curve during the Einstein crossing time $2t_E$. In contrast, in events of high magnification like the present one, most planetary perturbations are confined to a short time window on the order of the FWHM of the light curve (*5*). This reduces the number of degrees of freedom and permits a lower threshold value of $\Delta\chi^2$ to be used. Also, the photometry for the present study was carried out using the difference imaging technique (*13*). This uses all the information contained in the images of dense stellar fields to minimize systematic and statistical errors. fig. S2 shows light curves for various trials with $\Delta\chi^2$ at the threshold value superimposed on the data (*22*). Significant inconsistencies between these light curves and the data are seen.

Figure 2 shows exclusion regions for planets as a function of the planet:star mass ratio q and the projected separation from the lens star of M32/O219. These are the regions for which $\Delta\chi^2 >$ the threshold value given above. Figure 3 shows planetary detection efficiencies obtained by integrating the exclusion regions over the possible position angles (0° to 360°) of extrasolar planets. The efficiencies exceed 50% for $a = (0.80 - 1.25)r_E$ for $q = 10^{-5}$, and for $a = (0.32 - 3.0)r_E$ and $(0.05 - 21)r_E$ for $q = 10^{-4}$ and 10^{-3}, respectively. With the estimates given above, the q values 10^{-6}, 10^{-5}, 10^{-4}, and 10^{-3} correspond approximately to extrasolar planets of 1.3 times Mars mass, 1.3 times Earth mass, 1.0 times Uranus mass, and 1.3 times Saturn mass, respectively, and, as noted above, $r_E \approx 2.9$ AU. The observations therefore imply that planets slightly heavier than Earth are excluded from more than 50% of the projected annular region from approximately 2.3 to 3.6 AU surrounding the lens star of M32/O219, Uranus mass planets are excluded from 0.9 to 8.7 AU, and planets slightly heavier than Saturn are excluded from 0.2 to 60 AU.

Although no extrasolar planets were found in M32/O219, the observations eliminated the possible presence of terrestrial, ice-giant, and gas-giant planets over large ranges of orbital radii. If several microlensing events of high magnification can be detected and monitored, upper limits or rough statistics will be able to be determined on the abundances of these planets. A few events with magnification exceeding 100 are detected annually (*10*, *11*), and events with the very high magnification of M32/O219 may not be uncommon (*18*). Because our present knowledge of extrasolar planets is largely theoretical (*23*–*27*), any observational information should be helpful. Such information could also assist in the planning of future space-based probes of extrasolar planets (*28*–*30*).

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Supporting Online Material

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Direct Measurement of Light Waves

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The electromagnetic field of visible light performs ~10^{15} oscillations per second. Although many instruments are sensitive to the amplitude and frequency (or wavelength) of these oscillations, they cannot access the light field itself. We directly observed how the field built up and disappeared in a short, few-cycle pulse of visible laser light by probing the variation of the field strength with a 250-attosecond electron burst. Our apparatus allows complete characterization of few-cycle waves of visible, ultraviolet, and/or infrared light, thereby providing the possibility for controlled and reproducible synthesis of ultrabroadband light waveforms.

Although the wave nature of light has long been known, it has not been possible to measure directly the oscillating field of light. Radiation in the visible and higher frequency spectral ranges can so far only be characterized in terms of physical quantities averaged over the wave period. Nonlinear optical techniques now allow measurement of $\varepsilon_L(t)$, the amplitude envelope, and $\omega_L(t)$, the carrier frequency, as a function of time t, for light pulses with durations that approach the wave cycle (*1*, *2*). The carrier-envelope phase φ, which determines the timing between $\varepsilon_L(t)$ and $\omega_L(t)$, can also be measured (*3*). These measurements rely on carrier-envelope decomposition, which is physically meaningful only as long as the frequency spectrum of the wave is confined to less than one octave (*4*). If the radiation is composed of frequencies spanning a broader range (*5*–*17*), direct access to the field is required. Attosecond pulses of extreme ultraviolet (XUV) light were predicted to suit for this purpose (*18*, *19*). We report the direct measurement of the buildup and disappearance of the electric field of a light pulse through the use of an attosecond probe.

The electric field is defined as the force exerted on a point charge of unit value. Its conceptually most direct measurement must therefore rely on measurement of this force. In a light wave, the electric field E_L, and hence the force $F = qE_L$ it exerts on a particle with charge q, are subject to rapid variations. Access to this force is possible only if the probe charge is instantly placed in the field, i.e., within a time interval τ_{probe} over which the temporal variation of the force is "frozen", i.e., $\tau_{probe} \ll T_0 = (2\pi)/\omega_L$, where T_0 is the wave period. The probe charge can be launched into the field by knocking electrons free from atoms or ions instantly. In a linearly polarized wave, the change of the electrons' momentum $\Delta p(\vec{r}, t)$ at location $\vec{r}$ and time t along the direction of the electric field is given by

$$\Delta p(\vec{r},t) = e\int_{t}^{\infty} E_L(\vec{r},t')\mathrm{d}t' = eA_L(\vec{r},t) \quad (1)$$

where e is the electron charge and $A_L(\vec{r},t)$ is the vector potential of the electric field $E_L(\vec{r},t) = E_0\varepsilon_L(\vec{r}, t)\cos(kz - \omega_L t + \varphi)$, where E_0 is the maximum field amplitude, and k is the wave vector. In our analysis, we assumed the wave to propagate along the z direction, and $t = t_{real} - z/v_g$ was defined in a retarded frame to yield $t = 0$ as locked to the peak of the pulse travelling at the group velocity v_g.

The relation $E_L(\vec{r},t) = -\partial A_L(\vec{r},t)/\partial t$ implies that measuring the momentum boost $\Delta p(\vec{r},t)$ imparted to the freed electrons by the field at the location $\vec{r}$ at two instants differing in time by $\delta t \ll T_0/4$ will yield the electric field strength and direction directly as $E_L(\vec{r},t) = [\Delta p(\vec{r},t - \delta t/2) - \Delta p(\vec{r},t + \delta t/2)]/e\delta t$. This measurement procedure relies on a momentary release of the electrons within $\tau_{probe} \leq T_0/4$. For near infrared, visible, and ultraviolet light, this condition dictates that $\tau_{probe} < 1$ fs. Varying the timing of such a subfemtosecond electron probe across the laser pulse provides complete information on the electric field of the light wave.

These considerations suggest that the electron probe needs to be localized not only in time to a tiny fraction of the wave period T_0, but also in space to a tiny fraction of the wavelength λ_L of the light wave to be measured. The latter requirement can be substantially relaxed if we trigger the electron release with an energetic photon pulse that copropagates with the laser wave in a collinear beam (Fig. 1). Because the timing of the probe electrons relative to the light field is invariant to space in this case, in a gently focused laser beam they can be released and are subsequently allowed to move over distances substantially larger than λ_L, in a volume within which the spatial variation of the field amplitude $\varepsilon_L(\vec{r},t)$ is negligibly small for a fixed value of t.

Putting the above concept into practice requires the electron probe to be scanned through the entire laser pulse. For each newly set timing t, measurement of the momentum shift $\Delta p(t)$ of the probing electrons requires the laser pulse to pass through the measurement apparatus again. Full characterization of the light waveform is therefore only feasible if it can be reproducibly generated for repeated measurements. Another equally important prerequisite for implementation of the above concept is the availability of an energetic instantaneous excitation (for launching the probing electrons) that is not only confined temporally to a fraction of 1 fs but is also synchronized to the light wave with similar

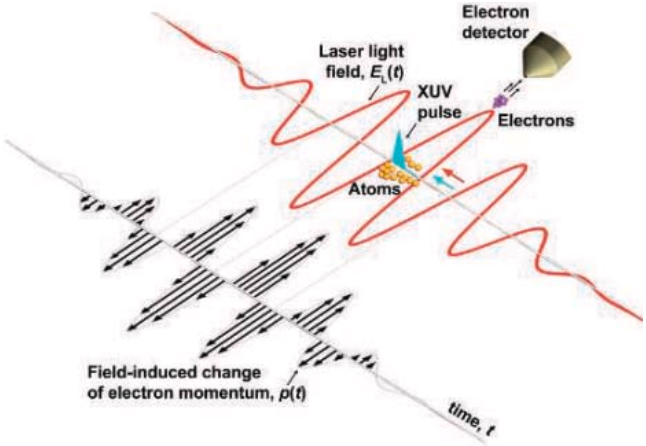

Fig. 1. Schematic of the measurement principle. A few-cycle pulse of laser light, together with a synchronized subfemtosecond XUV burst, is focused into an atomic gas target. The XUV pulse knocks electrons free by photoionization. The light electric field $E_L(t)$ to be measured imparts a momentum change to the electrons (black arrows), which scales as the instantaneous value of the vector potential $A_L(t)$ at the instant of release of the probing electrons. The momentum change is measured by an electron detector, which collects the electrons ejected along the direction of the linearly polarized $E_L(\vec{r},t)$.

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accuracy. With the generation of waveform-controlled, intense, few-cycle light pulses (*20*) and their successful application to producing single 250-as XUV pulses synchronized to the driver light wave (*21*), these preconditions are now fulfilled. The waveform-controlled pulses—after having produced the attosecond photon probe—allow through nonlinear optical frequency conversion the synthesis of reproducible, synchronized, ultrabroadband, few-cycle waveforms (*5–17*). These can be repeatedly sent into the measurement apparatus with exactly the same waveform, and the subfemtosecond XUV pulse is able to produce the electrons by photoionization for probing the oscillating light field with sufficient temporal resolution.

The electrons knocked free from the atoms by the XUV pulse can be most conveniently detected if the direction of their movement is left unchanged by the light field. This applies if electrons are detected within a narrow cone aligned with the electric field vector of the linearly polarized laser wave along the x direction and are ejected with a large-enough initial momentum p_i to fulfill $|p_i| > |\Delta p_{max}|$, where Δp_{max} is the maximum momentum shift induced by the field. A large initial momentum also benefits the measurement by enhancing the change of the electrons' kinetic energy ΔW, according to $\Delta W \approx (p_i/m)\Delta p$, and m is the electron's mass. This expression, together with Eq. 1, implies that the energy shift scales linearly with both the electric field and the wavelength of the light field to be probed (*22*). The importance of a large ΔW lies in the facts that the probing electrons are emitted with an inherent uncertainty $\delta W_{probe} \approx \hbar/\tau_{probe}$ (where $\hbar$ is Planck's constant h divided by 2π) and that the dynamic range over which the light field strength can be reliably measured scales with $\Delta W_{max}/\delta W_{probe}$ (ΔW_{max} is the maximum shift in the pulse).

Measurement of $E_L(t)$ over a substantial dynamic range requires a ΔW_{max} of several tens of electron volts. For an initial kinetic energy of $W_i \approx 100$ eV, this condition is satisfied for $E_0 < 10^8$ V/cm for near-infrared light and requires $E_0 \approx 3 \times 10^8$ V/cm for ultraviolet light (*22*). Noble gases with a low atomic number (such as helium and neon) safely resist ionization by a few-cycle field at these field strengths (*23*). The accuracy of definition of the location $\vec{r}$ is dictated by the size of the volume within which $\varepsilon(\vec{r},t)$ is approximately independent of $\vec{r}$. If the field is probed in the beam focus, this condition requires the probing electrons to be confined—during their interaction with the laser field—laterally (xy) and longitudinally (z) to a small fraction of the diameter and to the confocal parameter of the beam, respectively.

In a proof-of-concept experiment, we directly measured the $E_L(t)$ of the few-cycle laser pulse used for producing the attosecond photon probe (Fig. 1). Linearly polarized, waveform-controlled, <5-fs, 0.4-mJ, 750-nm ($T_0 = 2.5$ fs) laser pulses (*20*), with carefully optimized values of φ and E_0, produce single 250-as XUV pulses at $(\hbar\omega_{xuv})_{mean} = 93$ eV in a gas of neon atoms (*21*). The XUV pulse copropagates with the laser pulse in a collinear, laserlike beam to a second neon target placed in the focus of a spherical, two-component, Mo/Si multilayer mirror (*21*). The mirror, of 120-mm focal length, reflects XUV radiation over a band of ~9 eV, centered at ~93 eV. Consequently, the XUV pulse sets electrons free by photoionization with an initial kinetic energy of $p_i^2/2m = \hbar\omega_{xuv} - W_b$, (where W_b is the electron's binding energy) spread over an ~9-eV band, implying that $\delta W_{probe} \approx 9$ eV. The electrons' energy shift $\Delta W(t) \approx e(p_i/m)A_L(t)$ probes the laser vector potential. The volume of light-field probing is defined laterally by the <10-μm diameter of the XUV beam at its waist and longitudinally by the <50-μm size of the neon jet, which is well confined within the focal volume of the laser beam (diameter, >60 μm; confocal parameter, >5 mm). For $p_i^2/2m \approx 100$ eV, the electrons traveled less than 1 μm within 100 fs and hence remained safely confined to the region of constant laser field amplitude.

The field-induced variation of the final energy spectrum of the probe electrons versus delay between the XUV burst and the laser pulse (Fig. 2) reveal, without the need of any detailed analysis, that probing is implemented by a single burst of subfemtosecond duration that is synchronized with subfemtosecond accuracy to the measured laser field. $E_L(t)$ can now be directly (i.e., without any iterative steps) obtained through the procedure outlined above (Fig. 3). From the measured spectrum of the few-cycle laser pulse (Fig. 3, inset), we calculated $E_L(t)$ by a simple Fourier transformation on the assumption of absence of spectral phase variations. The result, with E_0 and φ chosen to yield the best match to the measured values, is shown in gray. The excellent fit to the measured field evolution indicates a near-transform-limited pulse. Its duration was evaluated as 4.3 fs, in good agreement with the result of an autocorrelation measurement.

It has been predicted by theory that the few-cycle pulse pumping the XUV source has a "cosine" waveform ($\varphi \approx 0$) if a single subfemtosecond pulse emerges from the ionizing atoms (*24*). Our results (Fig. 3) yield the exper-

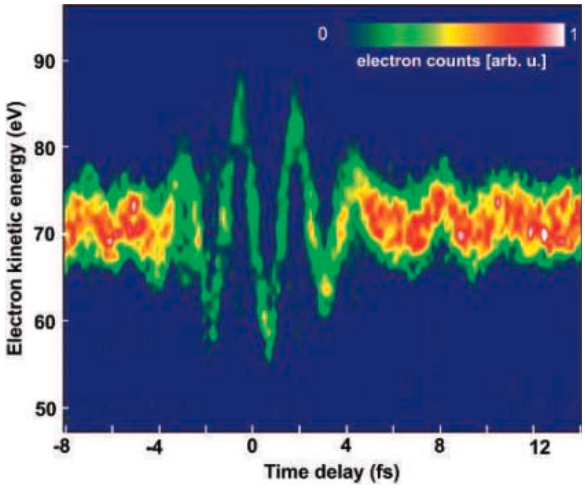

Fig. 2. A series of kinetic energy spectra of electrons detached by a 250-as, 93-eV XUV pulse from neon atoms in the presence of an intense <5-fs, 750-nm laser field, in false-color representation. The delay of the XUV probe was varied in steps of 200 as, and each spectrum was accumulated over 100 s. The detected electrons were ejected along the laser electric field vector with a mean initial kinetic energy of $p_i^2/2m \approx \hbar\omega_{xuv} - W_b =$ 93 eV – 21.5 eV = 71.5 eV. The energy shift of the electrons versus the timing of the XUV trigger pulse that launches the probing electrons directly represents $A_L(t)$. arb. u., arbitrary units.

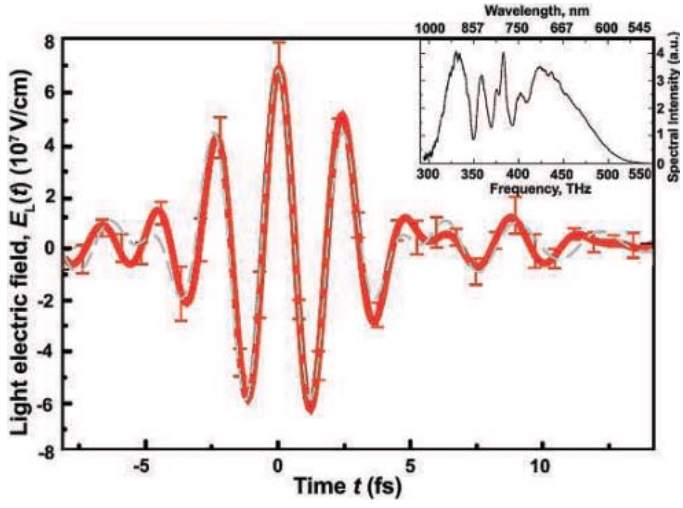

Fig. 3. $E_L(t)$ reconstructed (red line) from the data depicted in Fig. 2 and calculated (gray line) from the measured pulse spectrum (inset) with the assumed absence of a frequency-dependent phase and with E_0 and φ chosen so as to afford optimum matching to the measured field evolution. a.u., arbitrary units.

imental evidence. From this measurement, we also learn that the electric field points toward the electron detector at the pulse peak and that its strength is $\sim 7 \times 10^7$ V/cm. With the temporal evolution, strength, and direction of $E_L(t)$ measured, we have performed a complete characterization of a light pulse in terms of its classical electric field.

Direct probing of light-field oscillations represents what we believe to be a substantial extension of the basic repertoire of modern experimental science. The door to practical applications is opened by the creation of the key element of the demonstrated light-field detector, the synchronized attosecond electron probe, in a noninvasive manner. In fact, our intense <5-fs laser pulse appears to be capable of producing the necessary XUV trigger burst without suffering any noticeable back-action to its own temporal shape (Fig. 3). After having produced the attosecond photon probe, this powerful few-femtosecond pulse is ideally suited for the synthesis of ultrabroadband, few-cycle, optical waveforms (*5*–*17*). Being composed of radiation extending from the infrared through the visible to the ultraviolet region, the resultant few-cycle, monocycle, and conceivably even subcycle waveforms will offer a marked degree of control over the temporal variation of electric and magnetic forces on molecular and atomic time scales.

These light forces, in turn, afford the promise of controlling quantum transitions of electrons in atoms and molecules and—at relativistic intensities—their center-of-mass motion. Reproducible ultrabroadband light wave synthesis, a prerequisite for these prospects to materialize, is inconceivable without subfemtosecond measurement of the synthesized waveforms. Beyond providing the subfemtosecond electron probe for these measurements, the substantial experimental efforts associated with the construction and reliable operation of a subfemtosecond photon source will pay off in yet another way. The envisioned control of electronic motion with light forces can only be regarded as accomplished once it has been measured. Owing to their perfect synchronism with the synthesized light waveforms, the subfemtosecond photon probe will allow us to test the degree of control achieved by tracking the triggered (and hopefully steered) motion in a time-resolved fashion.

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Nanoribbon Waveguides for Subwavelength Photonics Integration

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Although the electrical integration of chemically synthesized nanowires has been achieved with lithography, optical integration, which promises high speeds and greater device versatility, remains unexplored. We describe the properties and functions of individual crystalline oxide nanoribbons that act as subwavelength optical waveguides and assess their applicability as nanoscale photonic elements. The length, flexibility, and strength of these structures enable their manipulation on surfaces, including the optical linking of nanoribbon waveguides and other nanowire elements to form networks and device components. We demonstrate the assembly of ribbon waveguides with nanowire light sources and detectors as a first step toward building nanowire photonic circuitry.

Photonics, the optical analog of electronics, shares the logic of miniaturization that drives research in semiconductor and information technology. The ability to manipulate pulses of light within sub-micrometer volumes is vital for highly integrated light-based devices, such as optical computers, to be realized. Recent advances in the use of photonic band gap (*1*, *2*) and plasmonic (*3*, *4*) phenomena to control the flow of light are impressive in this regard. One alternative route to integrated photonics is to assemble photonic circuits from a collection of nanowire elements that assume different functions, such as light creation, routing, and detection. Chemically synthesized nanowires have several features that make them good photonic building blocks, including inherent one-dimensionality, a diversity of optical and electrical properties, good size control, low surface roughness, and, in principle, the ability to operate above and below the diffraction limit. The toolbox of nanowire device elements already includes various types of transistors (*5*), light-emitting diodes (*6*), lasers (*7*, *8*), and photodetectors (*9*). An important step toward nanowire photonics is to develop a nanowire waveguide that can link these various elements and provide the flexibility in interconnection patterns that is needed to carry out complex tasks such as logic operations (*10*). Our demonstration of nanowire-based photonics complements and expands upon recent work on optical beam steering in mesostructured silica cavities (*11*) and on subwavelength structures made lithographically (*12*, *13*) and by the drawing of silica microfibers (*14*).

Nanoscale ribbon-shaped crystals of binary oxides exhibit a range of interesting properties including extreme mechanical flexibility, surface-mediated electrical conductivity (*15*), and lasing (*16*). As part of a recent study of the photoluminescence (PL) of SnO_2 nanoribbons, we noted that ribbons with high

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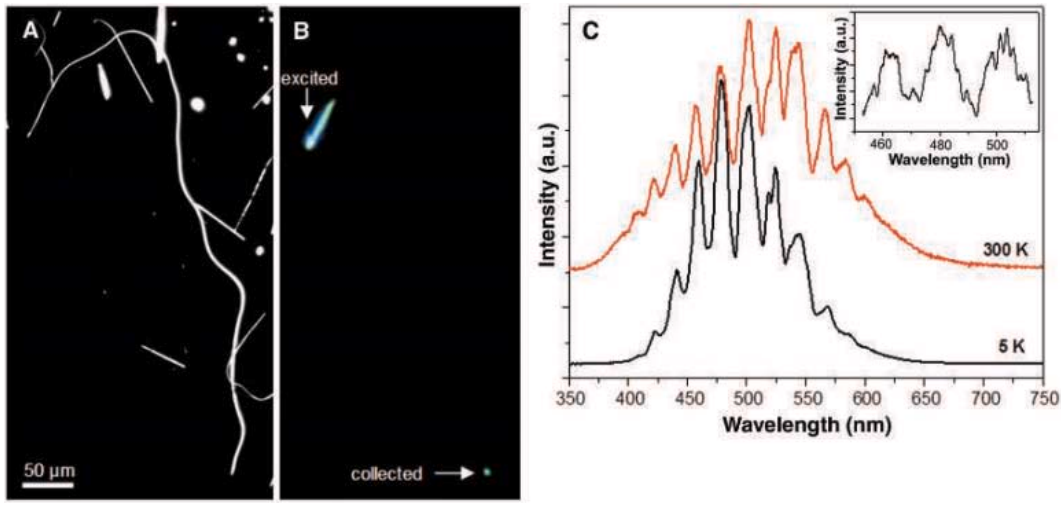

Fig. 1. Optical waveguiding in a 715-μm-long SnO_2 nanoribbon. (**A**) A dark-field image of the meandering ribbon (350 nm wide by 245 nm thick) and its surroundings. (**B**) The PL image of the waveguiding nanoribbon under laser excitation. The laser is focused to a spot size of ~50 μm (30° incidence angle) at the top end of the ribbon. (**C**) Spectra of the emission from the bottom terminus of the waveguide, collected at room temperature and 5 K. The mode structure does not change substantially with temperature, suggesting minimal dependence on index of refraction variations. A higher resolution emission profile (inset) shows fine structure in three of the central peaks. This fine structure is present in every peak. a.u., arbitrary units.

aspect ratios (>1000) act as excellent waveguides of their visible PL emission. SnO_2 is a wide band gap (3.6 eV) semiconductor characterized by defect-related PL bands at 2.5 eV (green) and 2.1 eV (orange) and finds application in gas sensors and transparent electrodes. We used a thermal transport process (*17*) to synthesize single-crystalline nanoribbons of SnO_2 with lengths of up to 1500 μm. These structures possess fairly uniform (± 10%) rectangular cross sections with dimensions as large as 2 μm by 1 μm and as small as 15 nm by 5 nm. Many of the ribbons are 100 to 400 nm wide and thick, an optimal size range for efficient steering of visible and ultraviolet (UV) light within a subwavelength cavity.

The waveguiding behavior of individual nanoribbons dispersed on SiO_2 and mica substrates was studied with the use of far-field microscopy and spectroscopy (*18*). Figures 1 and 2 show representative data collected from single ribbons with lengths of 715 and 425 μm, respectively. When we focused continuous wave laser light (3.8 eV) onto one end of a ribbon, the generated PL was strongly guided by the cavity to emanate with high intensity at its opposite end, mimicking a conventional optical fiber. Ribbons that possessed sizeable surface defects (i.e., large step edges or attached particulates) scattered guided light in a series of bright spots along their lengths. Contact points between ribbons were often dark, although overlying ribbons sometimes acted as scattering centers (Fig. 2C).

Typically, an emission spectrum collected from the end of a ribbon features complex, quasi-periodic modulation (Fig. 1C) that results from the interference of electromagnetic waves resonating within the rectangular cavity (i.e., an optical mode structure). In short nanowire waveguides, such modulation is attributed to longitudinal Fabry-Perot–type modes, with a mode spacing, $\Delta\lambda$, given by $\Delta\lambda = \lambda^2/\{2L[n - \lambda(dn/d\lambda)]\}$, where λ is the wavelength, L is the cavity length, and n is the index of refraction (2.1 for SnO_2). The nanoribbons, however, are so long that $\Delta\lambda$ is below the resolution limit of our instrument (0.1 nm). In addition, SnO_2 cavities are unlikely to show longitudinal modes, because the reflectivity of their end facets is low (≤13%) and there is no gain to compensate for scattering and output-coupling losses. We have yet to identify the observed modulation with specific transverse or bow-tie (*19*) modes. A systematic study of the spectral structure is complicated by the intricate dependence of the modes on ribbon cross-sectional size and orientation (through bend losses, substrate coupling, and variations in refractive index) as well as on light intensity and end facet roughness. We note that the existence of a mode structure indicates that nanoribbon cavities can have high finesse and show that the transmission at given wavelengths can be modified by distorting the cavity shape. Numerical simulations are now being applied to better understand the origin of this wavelength modulation.

In general, one would expect a subwavelength waveguide to show a large optical loss that is highly wavelength-dependent, with better confinement of shorter wavelength radiation. We illuminated single nanoribbons with monochromatic red, green, and blue light and established that red

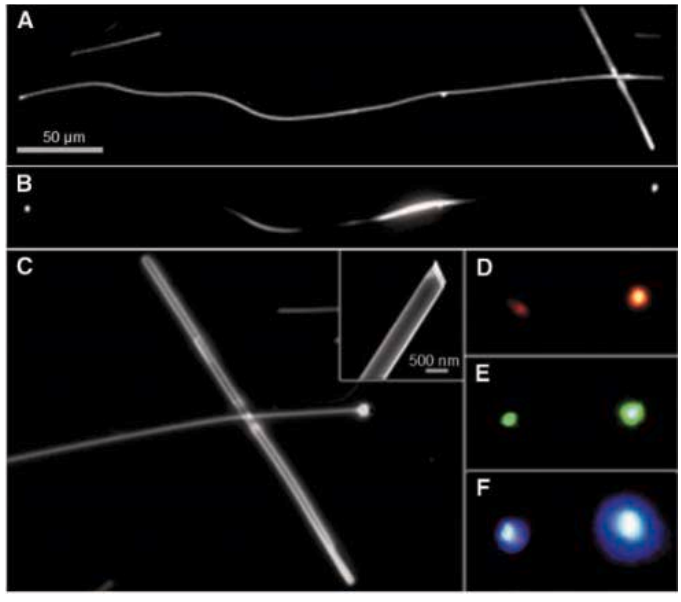

Fig. 2. Panchromatic waveguiding in a 425-μm-long ribbon. (**A**) Dark-field image. Cross-sectional dimensions are 520 nm by 275 nm. (**B**) PL image with the UV excitation spot centered near the middle of the ribbon, showing waveguided emission from both ends. (**C**) Magnified dark-field PL view of the right end, with the laser focused on the left end. A wide (~1 μm) ribbon lies across the ribbon of interest. (Inset) A scanning electron micrograph of the right terminus of the nanoribbon, showing its rectangular cross section. (**D** to **F**) Digital images of the guided emission during nonresonant excitation with monochromatic red, green, and blue light, respectively. The leftmost emission spot, caused by scattering at the ribbon-ribbon junction, can be eliminated by selectively removing the wide ribbon with the micromanipulator.

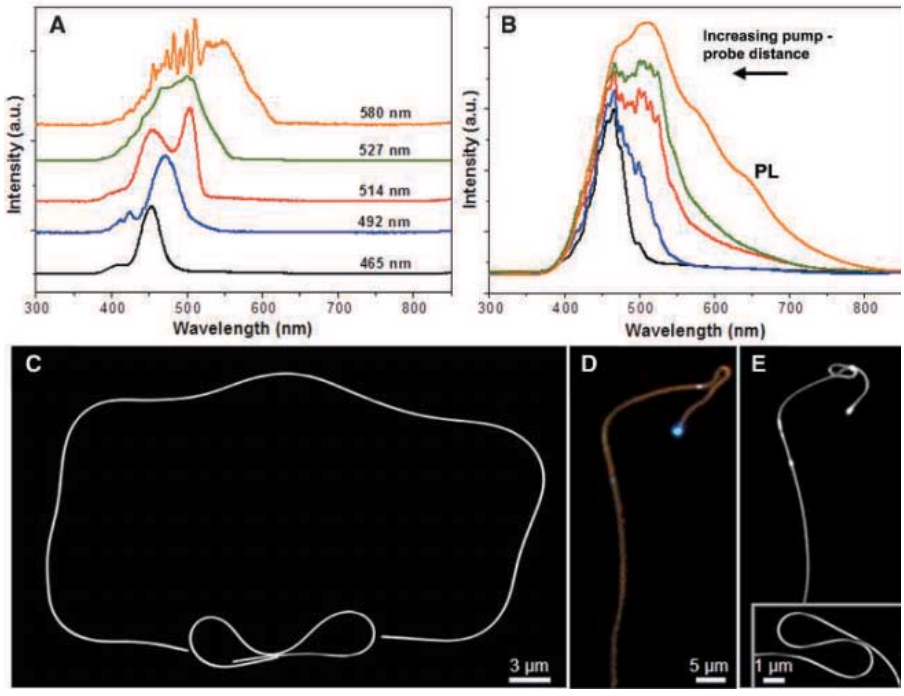

Fig. 3. Nanoribbon short-pass filters and shape manipulation. (**A**) Room-temperature PL spectra of five different nanoribbons, each 200 to 400 μm long, with 50% intensity cutoff wavelengths ranging from 465 to 580 nm. Cross-sectional dimensions of the 465, 492, 514, 527, and 580 nm filters are 310 nm by 100 nm (0.031 μm^2), 280 nm by 120 nm (0.034 μm^2), 350 nm by 115 nm (0.040 μm^2), 250 nm by 225 nm (0.056 μm^2), and 375 by 140 nm (0.052 μm^2), respectively. Spectra are normalized and offset for clarity. (**B**) A series of normalized emission spectra taken of a single nanoribbon (315 μm by 355 nm by 110 nm) as the pump spot was scanned away from the collection area. The unguided PL curve was obtained at a pump-probe separation of 50 μm. Larger separations result in a progressive loss of the long wavelengths. (**C**) An SEM image of a simple shape, demonstrating the high level of positional control afforded by the micromanipulator. This shape was created from a single straight ribbon (dimensions of 400 nm by 115 nm) that was cut into two pieces and then assembled. (D and E) Optical images of the emission end of a long nanoribbon (aspect ratio = 5200), showing the minimal effect of curvature on waveguiding. (**D**) A true-color photograph taken after crafting a single bend. (**E**) A black-and-white dark-field PL image captured after an S turn was completed. Blue light is guided around both 1 μm radii curves. An SEM image (inset) resolves the bent geometry. The scattering center on the bend is because of a step edge rather than physical contact.

waveguiding was rare; green, common; and blue, ubiquitous. For a given dielectric material and cavity geometry and wavelength, there exists a critical diameter below which all higher order optical modes are cut off and waveguiding becomes increasingly difficult to sustain. If a nanoribbon is treated as a cylinder of SnO_2 embedded in air, we find cutoff diameters for higher order transverse modes of about 270, 220, and 180 nm for the 652-, 532-, and 442-nm light used in our experiment (*20*). Although this approximation simplifies the cavity shape and ignores substrate coupling and other effects, these values are in reasonable agreement with scanning electron microscope (SEM) measurements of the blue and green waveguide sizes. Most of the ribbons in our samples are too thin to propagate red light over distances greater than 100 μm. However, sufficiently large ribbons guide wavelengths across the visible spectrum, acting as subwavelength red-green-blue optical fibers (Fig. 2, D to F).

The approximate size of a nanoribbon can be inferred from the color of its guided PL; large ribbons are white, whereas small ribbons are blue. When a ribbon of average size is pumped nearer to one end, it shines blue at the far end and green at the near end, demonstrating the higher radiation losses for longer wavelengths. This effect makes nanoribbons excellent short-pass filters with tunable cutoffs based on path length. We have identified ribbon filters spanning the 465- to 580-nm region that feature steep cutoff edges and virtually zero transmission of blocked wavelengths (Fig. 3, A and B).

We quantified the wavelength-dependent loss of long, straight ribbons with the use of near-field scanning optical microscopy (NSOM). Ribbons were pumped with a tightly focused laser beam (3.8 eV) at different points along their lengths relative to a NSOM collection tip held stationary over one of their ends. Directly exciting the semiconductor waveguide in this way created a consistent amount of light in the cavity for each measurement, avoiding the difficulty of inserting light from a second fiber with a constant insertion efficiency. Losses ranged from 1 to 8 dB mm^{-1} for wavelengths between 450 and 550 nm, depending on ribbon cross-sectional area and the density of scattering centers. These values are higher than those reported recently for subwavelength silica waveguides (*14*), mainly because of substrate-induced radiation loss and, in some cases, the existence of minor scattering crystal steps and terraces along the nanoribbon surface. We note, however, that the losses here are much better than what is required for integrated planar photonic applications, in which waveguide elements would transmit light over sub-micrometer distances.

The nanoribbons are of sufficient length and strength to be pushed, bent, and shaped with the use of a commercial micromanipulator under an optical microscope. Freestanding ribbons can be repeatedly and elastically curved into loops with radii as small as 5 μm, which is remarkable for a crystal that is brittle in its bulk form (*21*). On appropriately chosen surfaces, single ribbons are easily fashioned into a variety of shapes with the help of ribbon-substrate forces to prevent elastic recoil (Fig. 3C). Careful manipulation is normally nondestructive to the ribbon cavities. In practice, this manipulation method is applicable to nanostructures that are free to move and visible with dark-field microscopy, including, at the lower size limit, short nanowires (40 nm by 3 μm) and even large nanocrystals. Although an inherently slow serial process, it is faster and more versatile than similar approaches using, for instance, scanning probes (*22*) or in situ SEM manipulation (*23*). We can create networks of nanoribbon waveguides and build functioning optoelectronic components by assembling individual nanowire elements one at a time.

Manipulation also makes it possible to investigate the shape-dependent waveguiding of single nanoribbon cavities. For example, we fashioned a tight S turn in one end of a long, thin ribbon (dimensions of 785 μm by 275 nm by 150 nm) to illustrate the robust nature of optical steering in these structures (Fig. 3, D and E). Although losses around the bends could not be measured in this case, they were small enough to only minimally reduce light output from the end of the ribbon. In general, twists and bends with radii of curvature as small as 1 μm do not disrupt the ability of these subwavelength waveguides to channel light across hundreds of micrometers.

Bending a nanoribbon, even slightly, can dramatically change the mode structure of its output light (fig. S1). This is most likely

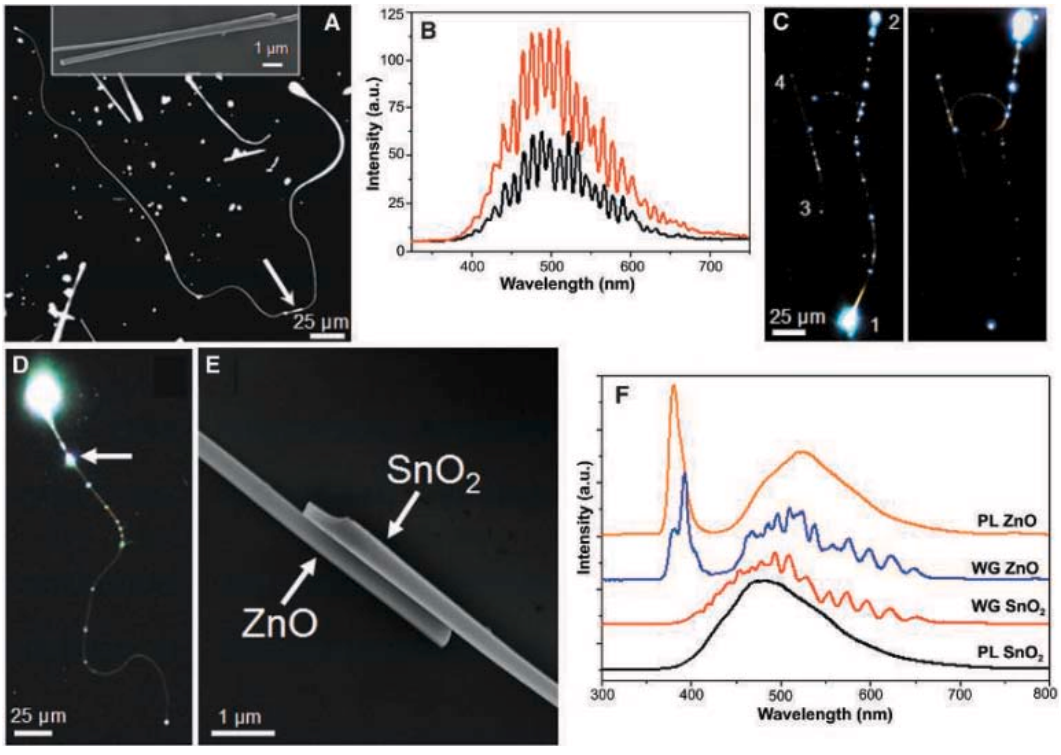

Fig. 4. Nanoribbon coupling and optical components. (**A**) A black-and-white dark-field PL image of two coupled ribbons (both ribbons are 750 nm by 250 nm, 630 μm total length). Light is incident on the right terminus of the right ribbon and collected at the left terminus of the left ribbon. The arrow denotes the location of the junction. An SEM image (inset) resolves the junction layout. (**B**) Raw emission spectra of the left ribbon before (red) and after (black) forming the junction. The addition of the second ribbon and the junction lowers the output light intensity by only 50%, whereas its modulation is retained. (**C**) True-color dark-field PL images of a three-ribbon ring structure that functions as a directional coupler. The ring ribbon (135 μm by 540 nm by 175 nm) is flanked by two linear ribbons (left, 120 μm by 540 nm by 250 nm; right, 275 μm by 420 nm by 235 nm). Light input at branch 1 exits preferentially at branch 3 (left), whereas light input at branch 2 exits branch 4 (right). See fig. S2 for a dark-field image of the structure. (**D**) A true-color dark-field PL image of a ZnO nanowire (56 μm long, at top, pumped at 3.8 eV) channeling light into a SnO_2 nanoribbon (265 μm long, at bottom). The arrow denotes the location of the junction. (**E**) An SEM image of the wire-ribbon junction. (**F**) Spectra of the coupled structures taken at different excitation and collection locations. From top to bottom: unguided PL of the nanowire, waveguided (WG) emission from the ZnO wire collected at the bottom terminus of the ribbon, waveguided emission from the SnO_2 ribbon excited just below the junction and collected at its bottom terminus, and unguided PL of the ribbon. The emission from the ZnO nanowire is modulated during its transit through the nanoribbon cavity.

because a change in cavity curvature and/or cavity-substrate coupling alters the interference pattern of propagating waves, resulting in the enhancement of some modes and the partial quenching of others. Our data also indicate that the emission pattern from a typical nanoribbon is spatially heterogeneous, as shown previously in ZnO nanowires (*24*). As a consequence, the far-field spectrum changes somewhat with collection angle, though not enough to account for the complex modal variations seen in response to distortions of the cavity shape.

Nanoribbon waveguides can be coupled together to create optical networks that may form the basis of miniaturized photonic circuitry. Because light diffracts in all directions when it emerges from a subwavelength aperture, nanoribbons must be in close proximity, and preferably in direct physical contact, to enable the efficient transfer of light between them. We tested various coupling geometries and found that a staggered side-by-side arrangement, in which two ribbons interact over a distance of several micrometers, outperforms direct end-to-end coupling, which relies on scattering between end facets. Staggered ribbons separated by a thin air gap can communicate via tunneling of evanescent waves (*25*). It is also possible to bond two ribbons together by van der Waals forces, often simply by draping one over another, to create a robust optical junction. Figure 4, A and B, shows an example of two-ribbon coupling. More functional geometries (*26*), such as Y junctions, branch networks, Mach-Zehnder interferometers, and ring oscillators can also be constructed. The three-ribbon ring structure in Fig. 4C operates by circulating light that is injected from one branch around a central cavity, which can be tapped by one or more output channels to act as an optical hub. With further integration, it should be possible to create optical modulators based on nanoribbon assemblies that use the electrooptic effect for phase shifting (*27*).

Nanowire light sources and optical detectors can be linked to ribbon waveguides to create input and output components for future photonic devices. Figure 4D shows light injection into a ribbon cavity by an optically pumped ZnO nanowire. The ribbon imprints its mode profile on both the UV and visible emission of the nanowire (Fig. 4F), demonstrating the propagation and modulation of a quasi-Gaussian light beam in a subwavelength optical cavity. In the opposite configuration, PL from a nanoribbon can be detected electrically by a ZnO nanowire positioned at its end (fig. S3). It is possible for ZnO to act as a detector in this case because it can weakly absorb sub–band gap light (*28*). We used a NSOM tip to excite the nanoribbon locally and thereby provide sufficient spatial resolution to detect waveguided light amid the background laser light scattered onto the wire detector. Scanning the NSOM tip on and off the ribbon caused photocurrent oscillations within the detector. Moreover, the oscillations ceased when the end of the ribbon was moved away from the nanowire detector. These results demonstrate the feasibility of nanowire-based photonic circuitry. Practical devices will require the integration of ribbon waveguides with electrically driven nanowire light sources and a variety of high-performance detector elements with different band gaps.

Single-crystalline nanoribbons are intriguing structures with which to manipulate light, both for fundamental studies and photonics applications. As passive elements, they are efficient UV and visible waveguides and filters that can be assembled into optical networks and components. Being semiconductors or, in their doped state, transparent metals, oxide nanoribbons are well suited to combine simultaneous electron and photon transport in active nanoscale components. Key challenges to the wider use of these materials include narrowing their size dispersity and devel-

oping better parallel assembly schemes for nanowire integration (*29*).

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Supporting Online Material

www.sciencemag.org/cgi/content/full/305/5688/1269/DC1
Materials and Methods
Figs. S1 to S3

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Transparent, Conductive Carbon Nanotube Films

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We describe a simple process for the fabrication of ultrathin, transparent, optically homogeneous, electrically conducting films of pure single-walled carbon nanotubes and the transfer of those films to various substrates. For equivalent sheet resistance, the films exhibit optical transmittance comparable to that of commercial indium tin oxide in the visible spectrum, but far superior transmittance in the technologically relevant 2- to 5-micrometer infrared spectral band. These characteristics indicate broad applicability of the films for electrical coupling in photonic devices. In an example application, the films are used to construct an electric field–activated optical modulator, which constitutes an optical analog to the nanotube-based field effect transistor.

Transparent electrical conductors pervade modern technologies, providing a critical component of video displays, video and still-image recorders, solar cells, lasers, optical communication devices, and solid-state lighting [for recent reviews, see (*1*, *2*)]. We describe a class of transparent conducting material based on continuous films of pure single-walled carbon nanotubes (SWNTs). These intrinsic electrical conductors are formed into uniform, optically homogeneous films of controllable thickness that are thin enough to be transparent over technologically relevant regions of the electromagnetic spectrum. Use of the transparent SWNT films (t-SWNTs) for current injection into p-GaN and for blue light–emitting GaN/InGaN diodes (light extracted through the films) has recently been demonstrated, together with patterning of the t-SWNTs by standard microlithographic techniques (*3*). Here we elaborate on the film production process, transfer to substrates, film morphology, and electrical and optical properties. We also demonstrate use of the t-SWNTs as the active element of an optical modulator. This constitutes an optical analog to the SWNT-based field-effect transistor (FET), modulating light transmission through the films by application of electric fields.

Other methods of transparent nanotube film production include drop-drying from solvent, airbrushing, and Langmuir-Blodgett deposition. These alternatives, however, present severe limitations in terms of the film quality or production efficiency (*4*). Our t-SWNT production process is quite simple, comprising three steps: (i) vacuum-filtering a dilute, surfactant-based suspension of purified nanotubes onto a filtration membrane (forming the homogeneous film on the membrane); (ii) washing away the surfactant with purified water; and (iii) dissolving the filtration membrane in solvent (*4*). Multiple techniques for transfer of the film to the desired substrate have been developed. The films can be made free-standing over appreciable apertures (~1 cm^2) by making the transfer to a substrate with a hole, over which the film is laid before membrane dissolution (*5*, *6*).

This filtration method has several advantages: (i) Homogeneity of the films is guaranteed by the process itself. As the nanotubes accumulate, they generate a filter cake that acts to impede the permeation rate. If a region becomes thicker, the local permeation rate and associated deposition rate slow down, allowing thinner regions to catch up. (ii) Because of their extreme rigidity (for objects of such small diameters), the nanotubes have long persistence lengths. They consequently tend to lie straight, gaining maximal overlap and interpenetration within the film as they accumulate (the curvature observed in Fig. 1D is likely caused by van der Waals forces dominating as the surfactant is washed away). This yields maximal electrical conductivity and mechanical integrity throughout the films. (iii) The film thickness is readily controlled, with nanoscale precision, by the nanotube concentration and volume of the suspension filtered.

Examples of the transparent films are shown in Fig. 1. Films of thickness 50 and 150 nm, as measured by atomic force microscopy (AFM) at step edges, display a corresponding increase in optical density (Fig. 1A). Films as large as 10 cm in diam-

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eter have been fabricated (Fig. 1B), but they could readily be made larger still. Film size is ultimately limited only by the dimensions of the filtration membranes, which are available in rolls as large as 30 cm by 10 m (Millipore). The t-SWNTs are highly flexible (Fig. 1C), with no observed degradation in their conductance after repeated flexure. Figure 1D shows the AFM image of a transparent nanotube film surface. The t-SWNTs have nanoscale porosity; however, for thicknesses greater than ~50 nm there are few straight, unobstructed paths through the network.

Figure 2 shows the transmittance spectrum for a 240-nm-thick, free-standing film over a broad spectral range and that for a 50-nm-thick film (on quartz) over a more limited range. The nanotubes are charge transfer–doped (acceptor-doped) by the nitric acid treatment used in their purification (*7*, *8*). This depletes electrons from valence-band van Hove singularities (see inset), reducing the rate of electronic transitions responsible for the absorption bands labeled S1, S2, and M1 (*9*). Heating the films to 600°C in inert gas desorbs the dopant, yielding the curves in which these absorption intensities are maximized (black curves). The transmittance going toward the far-infrared (IR) is limited by free carrier absorption (*7*). Such assignment is consistent with the lower transmittance in the mid-IR for the unbaked (hole-doped) film and with the increased transmittance there accompanying the loss of free carriers upon baking (dedoping). The as-prepared 50-nm film has transmittance greater than 70% over the visible part of the spectrum. In the near-IR at 2 μm, this film has transmittance greater than 90%. Use of Beer's law to scale the transmittance of the (unbaked) 240-nm film to a thickness of 50 nm indicates that the transmittance should remain >90% to just beyond 5 μm. Hence, such a film can be anticipated to have a window of >90% transmittance in a 2- to 5-μm spectral band.

The sheet resistance of the as-prepared 50-nm film was measured to be 30 ohm/square (resistivity 1.5×10^{-4} ohm·cm). Given the lack of index-matching antireflection coatings, this is a remarkably high transmittance for such low sheet resistance. For comparison purposes, the state-of-the-art mixed-oxide spinel $Ni_xCo_{x-1}O_{3/4}$ is more resistive (resistivity 3×10^{-3} ohm·cm) with a lower transmittance of 78% at 5 μm, achieved only after correcting for reflection losses, which is necessary because of the high refractive index of the material (*10*). Dedoped (baked) films are more transmissive further into the IR at the expense of some transmittance in the visible, and have resistivity about an order of magnitude higher than that of as-prepared, unbaked films. Note that the as-prepared films are not maximally doped, hence the 30 ohm/square sheet resistance does not represent a lower limit.

For transparent conductors, the plasma frequency marks the onset of high IR reflection. The dependence of the plasma frequency on carrier density, which also plays a critical role in the material's conductivity, results in a trade-off between conductivity and IR transparency. Much of the extensive research effort in traditional transparent conducting oxides focuses on changing the oxygen content or impurity doping during growth to modify the carrier concentration. The window of transparency is thereby optimized to the target spectral region while minimizing any trade-off in decreased conductivity. For the nanotubes, the ease of chemical charge-transfer doping to obtain such transparency-versus-conductivity optimization (via exposure of the nanotubes to vapors of appropriate chemicals) provides an additional advantage for the t-SWNTs. Moreover, charge transport in these t-SWNTs is p-type, unlike the far more common transparent conducting oxides [e.g., indium tin oxide (ITO)], which are n-type. This should permit new complementary applications and alternative photonic coupling schemes (*3*).

Chemical charge-transfer doping, which adds or removes electrons from the nanotubes, shifts their Fermi levels. Such

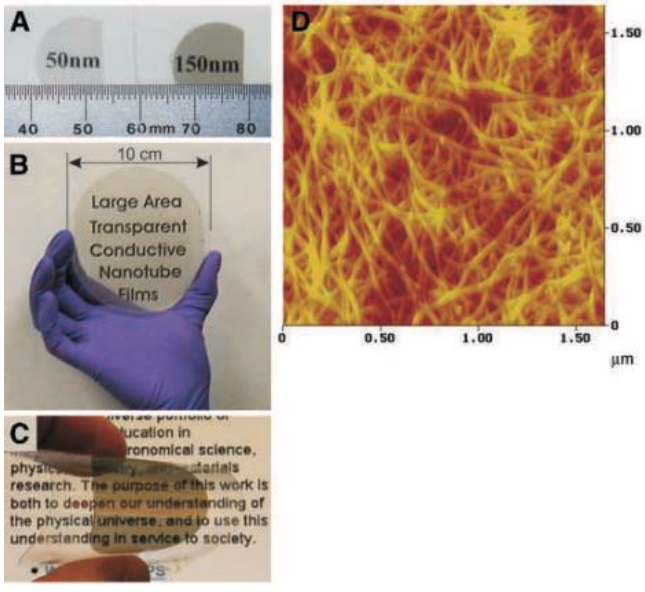

Fig. 1. Transparent SWNT films. (**A**) Films of the indicated thickness on quartz substrates. (**B**) A large, 80-nm-thick film on a sapphire substrate 10 cm in diameter. (**C**) Flexed film on a Mylar sheet. (**D**) AFM image of a 150-nm-thick t-SWNT film surface (color scale: black to bright yellow, 30 nm). The text in (A) to (C) lies behind the films.

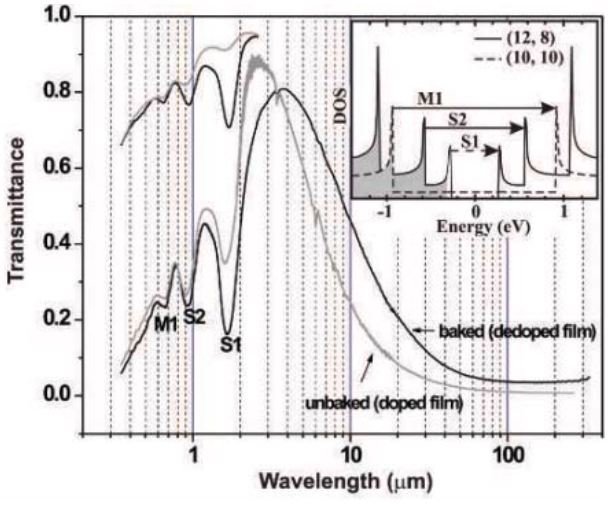

Fig. 2. Transmittance spectra for two t-SWNT films (doped and dedoped) of thickness 50 nm (on quartz) and 240 nm (free-standing). The curves with greater transmittance (upper left) are for the 50-nm film. Gray curves denote the charge-transfer, hole-doped films; black curves denote those films after dedoping. Inset shows the DOS for a representative (12,8) semiconducting nanotube (solid curve) and a superimposed (10,10) metallic nanotube (dashed curve) within a tight binding model. Arrows between singularities represent electronic transitions responsible for the S1, S2, and M1 absorption bands. Depletion of the first singularity (filled electronic states in gray) results in the loss of the corresponding electronic transition (dashed arrow) and loss of the associated S1 absorption intensity. The t-SWNT films consist of a mixture of semiconducting and metallic nanotubes with a distribution of diameters and chiral angles. The (*n*,*m*) index dependence of the spacing between van Hove singularities modulates the transition energies to yield the broad absorption bands seen in the spectra (also labeled S1, S2, and M1). Bundling of the nanotubes further broadens the observed absorption bands.

Fermi level shifts need not be induced chemically; they can also be induced by electric fields. In a nanotube-based FET (NFET), a semiconducting nanotube is electrically coupled to source and drain terminals while the field between the nanotube and an isolated gate electrode shifts the nanotube Fermi level, modulating its carrier concentration (*11*–*14*). In an electrolyte-gated NFET, the gate electrode is provided by an electrolyte in contact with a remote electrode (*15*, *16*). Applying a potential between the nanotube (via the source/drain terminals) and the remote electrode establishes an electric double layer consisting of the excess charge drawn onto the nanotube from the source/drain terminals compensated by the near-lying cloud of oppositely charged electrolyte ions. As long as the gate voltage is kept below potentials at which redox reactions occur, the ionic cloud of the electric double layer behaves like an exceptionally near-lying gate electrode.

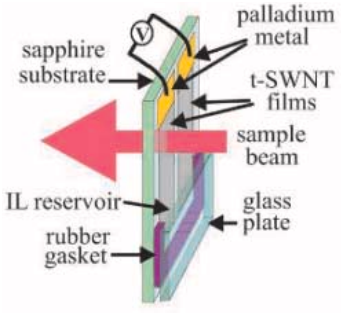

Fig. 3. Optical analog to the electrolyte-gated NFET (O-NFET).

Figure 3 shows a device schematic that constitutes an optical analog to the electrolyte-gated NFET—that is, it modulates light transmission through the device as a function of the electrolyte "gate" potential (*17*). The device consists of two adjacent t-SWNT films (each 150 nm thick) deposited onto a sapphire substrate. For electrical contact, each film has palladium metal (*18*) sputtered across one end. A U-shaped rubber gasket between the bottom portion of the substrate and a glass plate forms a reservoir into which the non–metal-coated end of each t-SWNT film extends (a clamp holding the plates together is not shown). While they are positioned horizontally, the films are saturated with the ionic liquid (IL) 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide. When the assembly is tipped up to lie vertically, excess IL drains into the reservoir. Because the IL wets the nanotubes, a thin layer, bridged by the IL drained into the reservoir, remains associated with each film. Monochromatic light from the sample beam of a Perkin-Elmer Lamba 900 spectrophotometer is passed through only one of the SWNT films. The second film provides a "gating" counterelectrode with nanoscale surface area comparable to that of the optically probed film. A counterelectrode with smaller surface area would limit the capacitance, decreasing the charging efficiency of the probed film. The density of electronic states (DOS) for the nanotubes (Fig. 2, inset) illustrates the idea behind the device. A negative potential applied to the gating (counterelectrode) film depletes electrons from the van Hove singularity associated with the S1 electronic transitions for the probed film. This results in a loss of the corresponding absorption and increased optical transmission through the device at the associated wavelength.

Figure 4 shows the optical transmittance for the optical NFET (O-NFET) illustrated in Fig. 3 as a function of voltage applied between the films. At the S1 absorbance maximum (1676 nm), the transmittance is modulated from 44% to 92% between "gate" (counterelectrode) potentials of ±1.8 V (*19*–*23*). Further in the IR at 3080 nm, the modulation is from 97% to 75% over the same voltage range. Relative to the changes in the S1, S2, and M1 bands, transmittance changes at wavelengths greater than ~2000 nm occur in the opposite direction with voltage. Negative counterelectrode potentials draw excess holes onto the probed film, increasing the free carrier absorption and reducing the transmission, whereas positive counterelectrode potentials reduce the hole concentration, decreasing the free carrier absorption and increasing the transmission. These modulations in the transmittance are fully reversible, with no degradation observed after hundreds of cycles (*24*).

For the S1, S2, and M1 absorbance bands, the SWNT DOS (Fig. 2, inset) would suggest a symmetry between positive and negative applied potentials. Negative gate potentials should deplete the initial transition-state (valence band) singularities, decreasing the absorption intensities. Positive gate potentials should fill the terminal-state (conduction band) singularities. With fewer terminal states available

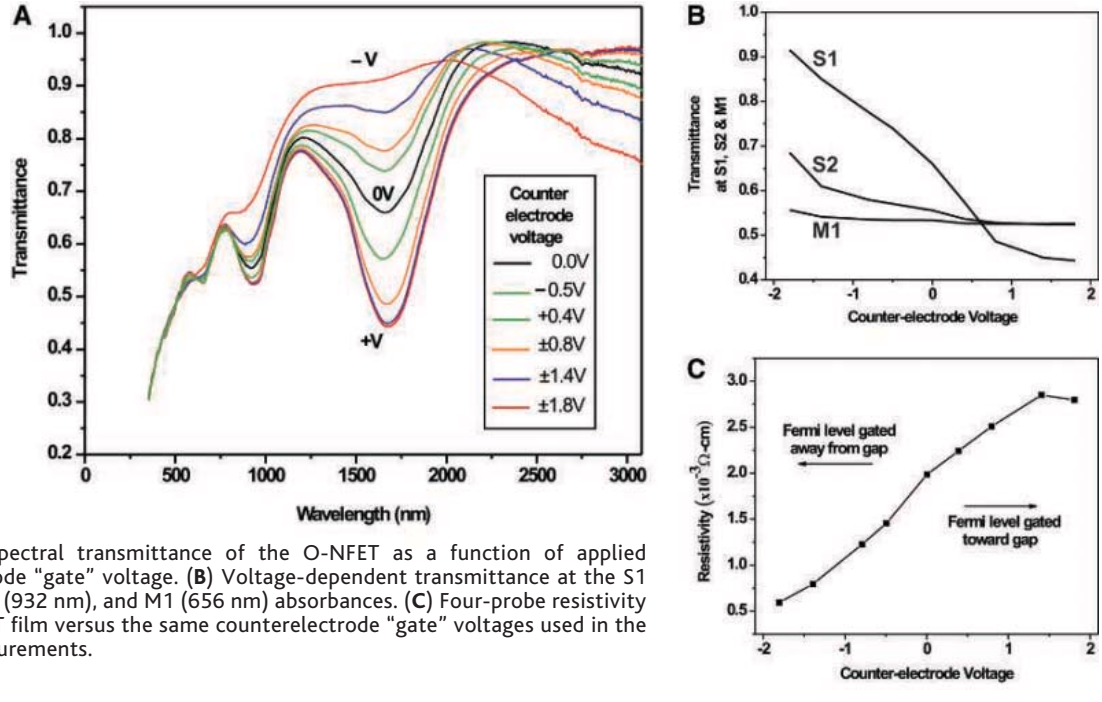

Fig. 4. (**A**) Spectral transmittance of the O-NFET as a function of applied counterelectrode "gate" voltage. (**B**) Voltage-dependent transmittance at the S1 (1676 nm), S2 (932 nm), and M1 (656 nm) absorbances. (**C**) Four-probe resistivity of the t-SWNT film versus the same counterelectrode "gate" voltages used in the spectral measurements.

for the transition, this should also decrease the absorption intensities. The corresponding behavior in an electronic NFET has the Fermi level lying in the gap and the conductance increasing for both positive and negative gate potentials, in which case the device is said to be ambipolar. The zero voltage curve for the O-NFET does not yield the maximum absorption intensities for the S1, S2, and M1 bands, as would be expected for the intrinsic Fermi level lying in the gap. Rather, positive gate voltages increase those absorption intensities, whereas negative gate voltages decrease those intensities. This p-doped–like behavior (which has the Fermi level of the semiconducting nanotubes underlying the S1 valence singularity at 0 V) appears despite the films having been dedoped (baked) before saturation of the t-SWNT films with the ionic liquid. One possible explanation for this seemingly intrinsic p-type behavior is equilibration of the chemical potentials among the nanotubes, the Pd electrodes, and the ionic liquid. Alternatively, impurities in the ionic liquid may lead to chemical charge-transfer doping of the nanotubes.

The simple model provided by the DOS (Fig. 2, inset) further suggests that the changes in the S1, S2, and M1 absorbance intensities should emerge sequentially as the Fermi level progresses sequentially through the corresponding valence band singularities. That is, changes in S1 should be complete before changes in S2 begin, followed (once the latter has been fully saturated) by changes in M1. As seen in Fig. 4B, which plots the transmittance at the S1, S2, and M1 absorbance peaks against the gate potentials, the changes in transmittance there clearly do not arise sequentially. This apparent inconsistency is explained by the fact that the nanotubes are bundled together in hexagonal close packing that excludes the large ionic liquid ions from the interiors of the bundles. With applied potential, ions of the double layer attract electronic countercharges to the outermost nanotubes of the bundles; these charges in turn partially screen the interior nanotubes from the ionic fields. Hence, for a given potential under the electrostatic equilibrium established, the Fermi level for nanotubes on the exterior of a bundle can lie below the M1 valence singularity while that for the interior nanotubes can still lie within the S1 valence singularity. However, the low carrier density of the nanotubes makes their screening less than perfect, so that the S1 singularity—even for the interior nanotubes—can be nearly fully depleted, as indicated by the near-complete loss of the S1 absorption at the counterelectrode potential of –1.8 V.

We have also measured the four-probe resistivity of the t-SWNT films, while they are gated by the counterelectrode, at the potentials used in the optical transmittance measurements (*25*). When resistivity is plotted against gate voltage (Fig. 4C), the change in resistivity is consistent with a diminished carrier concentration as the Fermi level is gated toward the gap of the semiconducting nanotubes with increasing positive gate voltage. The saturation beyond 1.4 V corresponds to the semiconducting nanotubes no longer contributing to transport through the film. This behavior is also consistent with the saturation appearing in the S1 optical absorption intensity between 1.4 and 1.8 V; once the Fermi level for all the semiconducting nanotubes lies in the gap, the absorbance has already been maximized.

The simultaneous high transparency and good electrical conductivity of the t-SWNTs can be understood on the basis of three properties of the nanotubes: (i) low carrier density; (ii) high electronic mobility; and (iii) the suppression of light absorption and reflection for polarization components perpendicular to the nanotube axis, which reduces the optical density of the disordered SWNT films for unpolarized incident light. Such films are likely to find application as transparent conductors in the IR, where our measurements show them to have exceptional properties. It is too early to tell if they can compete in the visible part of the spectrum against ITO. Given their flexibility, however (ITO is comparatively brittle), they seem likely to at least find niche applications in, e.g., flexible/foldable displays. Devices like our O-NFET optical modulator may find application in spacecraft thermal control and military camouflage countermeasures (*26*).

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19. Modulation of the three principal SWNT absorption bands in a three-terminal electrochemical cell has been reported (*20*, *21*). There, the effect was ascribed to nanotube Fermi level shifts associated with intercalated species generated by electrochemical redox reactions in the electrolyte. The SWNT film (produced by airbrushing) used in those experiments evidently did not have sufficient intrinsic conductivity to be used without a thin, transparent platinum electrode (*20*) or ITO electrode (*21*) onto which the nanotubes were sprayed. The ionic liquid in our experiments acts merely as a near-lying gate electrode undergoing no complicating redox reactions. It also yields substantially cleaner SWNT spectra over broader voltage and spectral ranges. The spectra we show are raw data.
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23. Our all–solid-state device has similar spectral behavior with "gate" voltage; however, the magnitude of the modulation is much smaller (0.2% over ±6 V at the peak of S1) because electrostatic screening allows only the layer of nanotubes nearest the ITO counterelectrode to participate. Because gating is all electronic (as opposed to ionic), however, the response time is much faster than the ionic liquid device.
24. With the spectrophotometer in a mode that records the transmittance at fixed wavelength as a function of time, we sat on the peak of the S1 absorption band while driving the O-NFET with a square wave potential. No systematic changes in the amplitude of the modulation were observed over multiple measurements totaling several hundred cycles. Only small changes (a few percent) in the average transmittance, both up and down, were seen—entirely consistent with spectrometer drift over the long time scale of these measurements.
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Supporting Online Material

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SOM Text

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Evidence for Deep Magma Injection Beneath Lake Tahoe, Nevada-California

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A deep earthquake swarm in late 2003 at Lake Tahoe, California (Richter magnitude < 2.2; depth of 29 to 33 kilometers), was coeval with a transient displacement of 6 millimeters horizontally outward from the swarm and 8 millimeters upward measured at global positioning system station Slide Mountain (SLID) 18 kilometers to the northeast. During the first 23 days of the swarm, hypocentral depths migrated at a rate of 2.4 millimeters per second up-dip along a 40-square-kilometer structure striking north 30° west and dipping 50° to the northeast. SLID's transient velocity of 20 millimeters per year implies a lower bound of 200 nanostrains per year (parts per billion per year) on local strain rates, an order of magnitude greater than the 1996 to 2003 regional rate. The geodetic displacement is too large to be explained by the elastic strain from the cumulative seismic moment of the sequence, suggesting an aseismic forcing mechanism. Aspects of the swarm and SLID displacements are consistent with lower-crustal magma injection under Lake Tahoe.

The 12 to 14 mm/year of northwest-directed motion of the Sierra Nevada mountain range in eastern California and western Nevada relative to stable North America represents about 20 to 25% of the Pacific–North America plate motion budget (*1*, *2*). At the latitude of Lake Tahoe, California-Nevada, much of this shear and extension is concentrated in the westernmost Great Basin, characterized at the surface by strike-slip and normal faulting. The eastern boundary of the Sierra Nevada is a geologically young transition marked by north-striking, east-dipping normal fault systems that account for Great Basin extension, the westward evolution of the Sierra Nevada–to–Great Basin transition, and the consequent eastward collapse of the competent Sierra Nevada block. Paleozoic and Mesozoic roof pendants and Cretaceous granites in the region are overlain by volcanic rocks from the Miocene to about 3 million years ago (Ma) and by a distinct younger period, from 1 to 2 Ma, of localized rhyolitic and basaltic magmatism (*3*).

The shallow crust in the California-Nevada border region near Lake Tahoe includes north-south–striking normal faults and northeast- and northwest-striking strike-slip faults operating within east-west–oriented regional extension (σ_3). This is a consequence of the near equivalence of the maximum and intermediate (σ_1 and σ_2) compressive stresses (*4*, *5*). The base of the seismogenic zone in the region varies locally from about 15 to 18 km (*6*). In the Lake Tahoe area, no crustal earthquakes deeper than 20 km can be identified from more than 25 years of monitoring.

In a map view, the deep crustal sequence of earthquakes observed in 2003 straddles the northwest shore of Lake Tahoe and defines a planar structure of 8 by 5 km striking N30°W and dipping 50°NE between depths of 29 and 33 km (Fig. 1 and fig. S1). A total of 1611 earthquakes were located in the swarm [sum of the moment magnitude (M_w) of all events is 3.1], and the 1179 best-located events are shown [supporting online material (SOM) text]. The swarm began with a 0.0-magnitude event on 12 August 2003 and continued through 19 February 2004. Fifteen earthquakes on 31 December 2003 and 1 January 2004 marked the last days with more than one located event, and the last events of the swarm (as of 26 July 2004) occurred on 5, 8, 12, and 20 January and 19 February 2004. Daily activity rates are peaked at times when the earthquake depths are shallower (Fig. 2). The final temporal concentration of seismicity began on 22 November 2003 and peaked with 88 earthquakes on 27 November 2003 (Fig. 2A). Seismograms of the deep events resemble shallow tectonic earthquakes near Lake Tahoe that have impulsive *P*-wave arrivals and high-frequency waveforms. However, no long-period (LP) earthquakes, generally thought to result from magma movement in the crust, have been identified.

Hypocentral depths progressed from about 33 to 29 km (relative to the elevation of Lake Tahoe) by 3 September 2003 at a rate

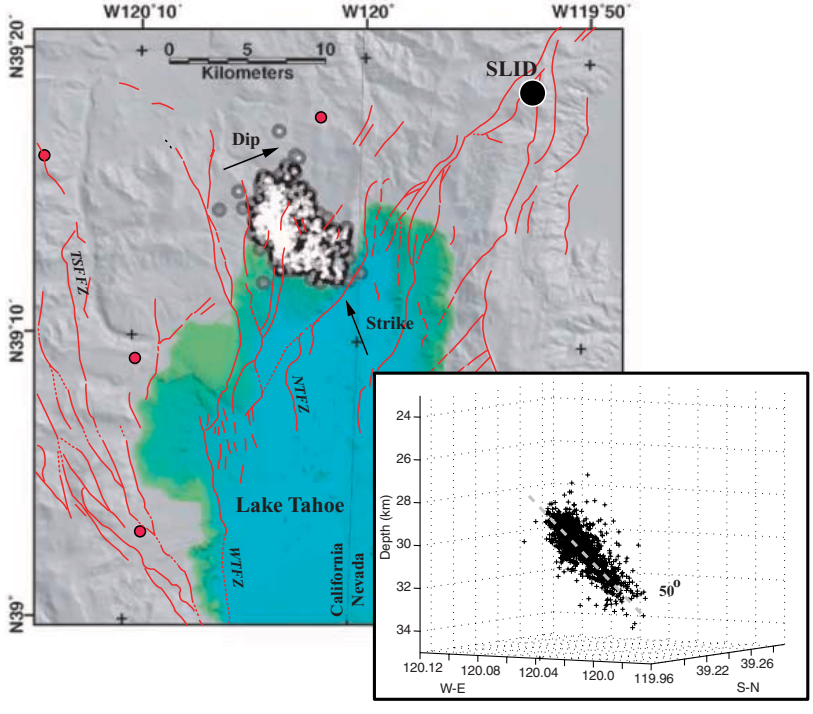

Fig. 1. Deep earthquake activity (>20 km) in the Lake Tahoe, California area, 2003 to 2004, and location of GPS station SLID and faults with Holocene displacement (*8*). Red circles mark seismograph stations. Major east-dipping normal faults: TSFFZ, Tahoe-Sierra frontal fault zone; WTFZ, West Tahoe fault zone; NTFZ, North Tahoe fault zone. Inset shows cross-sectional view along strike, N30°W, of inferred structure at depth.

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(±SD) of 2.4 ± 0.6 mm/s (8.5 m/hour) up-dip along the imaged planar structure (Fig. 2B). The temporal and spatial depth distribution implies a source propagating up-dip that had reached its shallowest extent by 3 September 2003, 23 days into the sequence (Fig. 2B). This is consistent with the leading edge of a volcanic dike intrusion where earthquakes are triggered by high strain rates and localized stresses at the injection front (*7*, *8*).

An increase in the upper crustal seismicity (depth of <18 km) began about 2 months after the initiation of the deep-crustal sequence (fig. S2) and continued through June 2004. The largest of the shallow events occurred on 3 June 2004: an M_w 4.2 earthquake at a depth of 8.5 km, about 10 km north-northeast of the epicentral region of the deep swarm. Including the 2004 event, the Nevada Seismological Laboratory catalog lists eight earthquakes with Richter magnitudes (M_L) ≥ 4.2 since 1950 within 30 km of the center of North Lake Tahoe. The mean rate is one event this size or larger every 6 to 7 years. The Coulomb failure function on shallow faults was probably altered, consistent with the increase in shallow seismicity.

Magnitudes for the Lake Tahoe deep swarm range from M_L −0.2 to 2.2 with a *b* value of 2.0 (SOM text) (*b* is the slope in the regression equation $\log_{10} N = a - b\,M$, where *N* is the number of events at magnitude *M*). When *b* values are much greater than 1.0, they are anomalous for upper-crustal tectonic earthquakes but typical of volcanic regions (*9*, *10*). In the Long Valley volcanic area, Wiemer *et al*. (*11*) found *b* values as high as 1.8 for upper-crustal sequences associated with upper-crustal volcanic processes.

Double-couple focal mechanism solutions have been determined for the 24 largest events (M_L > 1.5) with a combination of *P*-wave first-motion polarities and *P*- and *S*-wave amplitudes (fig. S3 and SOM text). With one exception, all have a reverse-faulting component. Most solutions are consistent with zones of weakness moved to failure by a maximum compressive stress oriented 225° and plunging 30°SW (fig. S4). The maximum compressive stress (σ_1) is aligned approximately normal to the imaged structure, consistent with tensile failure along the northeast-dipping structure (*7*). Among the reverse-faulting events, the *T* axes strike northeast, but over a wide range (fig. S4). This is in contrast to regional east-west–oriented extension observed in upper-crustal focal mechanisms that are consistent with normal fault orientations near Lake Tahoe (*4*, *12*). A possible explanation is that the stress field is locally perturbed by processes within the volume of the swarm.

A continuously recording geodetic global positioning system (GPS) station on the summit of Slide Mountain (SLID, Fig. 1) is located horizontally 18 km away at N60°E from the center of the swarm region and 31 km obliquely from the center of the northeast-dipping imaged planar structure at depth, nearly perpendicular to the plane. SLID is part of the 53-station Basin and Range Geodetic Network (BARGEN), which has operated continuously since 1996 to investigate tectonic deformation in the Basin and Range Province (*2*, *13*). The same instrument design (including receiver, antenna, radome, and deep-anchored braced monument) has been implemented at all BARGEN stations in the region of SLID without changes since December 1999. Therefore, our geodetic analysis started on 1 January 2000, including data through 28 June 2004.

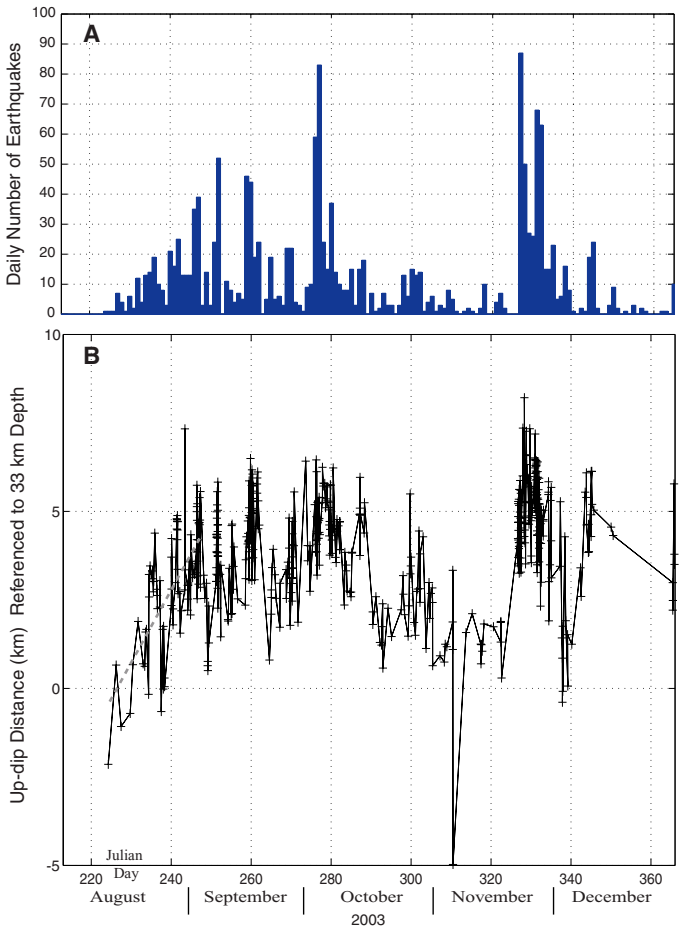

Fig. 2. (**A**) Daily number of earthquakes for all located deep events. (**B**) Temporal progression of earthquake depths relative to 33-km depth along up-dip distance of lower-crustal inferred structure. The dashed line is a rate of 2.4 mm/s from 12 August through 3 September 2003.

GPS data from SLID were processed with data from the five nearest BARGEN stations (UPSA, GARL, SHIN, GABB, and TUNG; 99 to 184 km from SLID in Fig. 4) in 24-hour batches with the GIPSY OASIS II software to produce six time series of three-dimensional (3D) precise point positions (longitude, latitude, and ellipsoidal height) relative to ITRF2000 (*14*–*16*). Each station's coordinate time series was detrended and then regionally filtered (*17*) by subtracting the mean time series from the five neighboring stations. Annual periodic signals were then removed (*18*), and finally 7-day averages were formed (Fig. 3). The estimated annual signals have a mean amplitude of 0.3 mm in horizontal components and 0.9 mm in height. The weekly time series have a 1-SD scatter of 0.5 mm in horizontal components and 2.1 mm in height, before July 2003. The scales of the formal error bars were adjusted to be consistent with this scatter (SOM text).

In contrast to neighboring BARGEN stations, all three SLID coordinates underwent episodic displacement starting in July 2003 and lasting 6 months, coeval with the deep crustal seismicity. The difference in mean coordinates between the periods from January to June 2004 and from January to June 2003 were taken as displacement estimates, yielding 3.1 ± 0.2 mm northward, 4.9 ± 0.3 mm eastward, and 7.9 ± 1.0 mm upward (error of 1 SD). The SLID 2D horizontal displacement of 5.8 mm is oriented N58°E, approximately in the direction of SLID relative to the source region, with the 3D vector displacement of 9.8 mm aligned approximately normal to the planar structure at depth (Fig. 1). In contrast, for the five neighboring stations the root mean square of estimated displacements is 0.4 mm for horizontal components, 0.7 mm for height, and 0.9 mm in total distance. These numbers provide a realistic estimate of the total

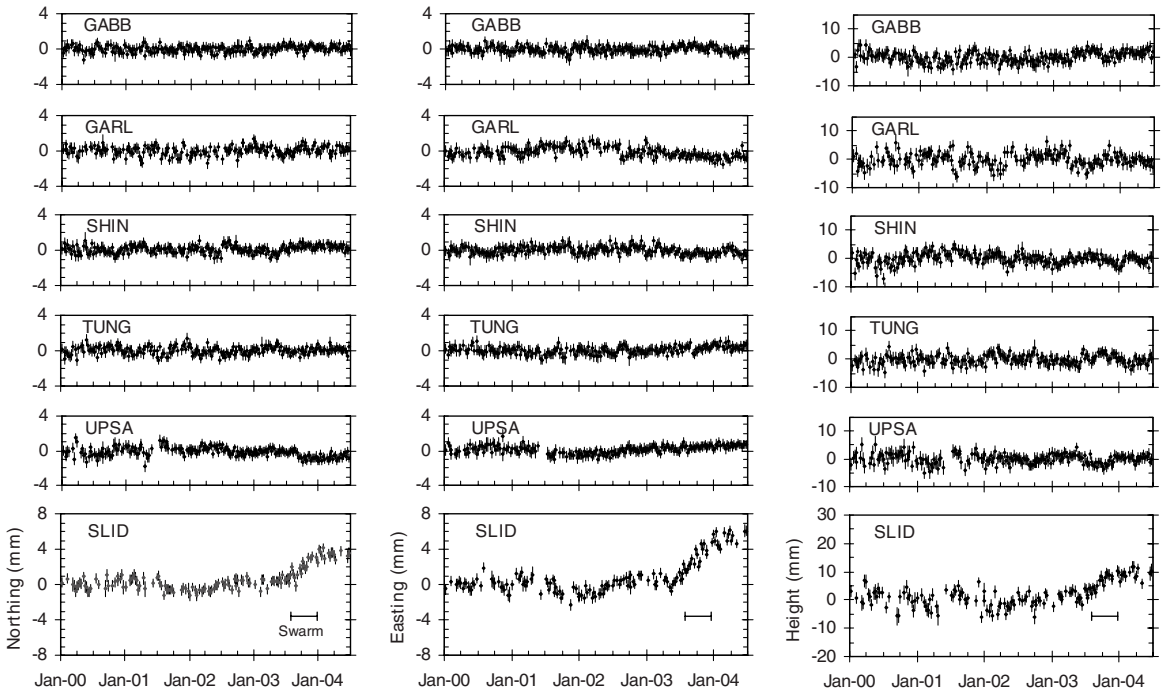

Fig. 3. GPS coordinate time series for SLID and neighboring stations in each of three component directions. Data displayed are 7-day averages with scaled formal error bars of 1 SD. Coordinate axes for SLID are extended to accommodate the signal, but the scale is the same for all stations for a given component. The scale of the height component is a factor of 3 greater than for the horizontal components to visually normalize the higher level of noise in height.

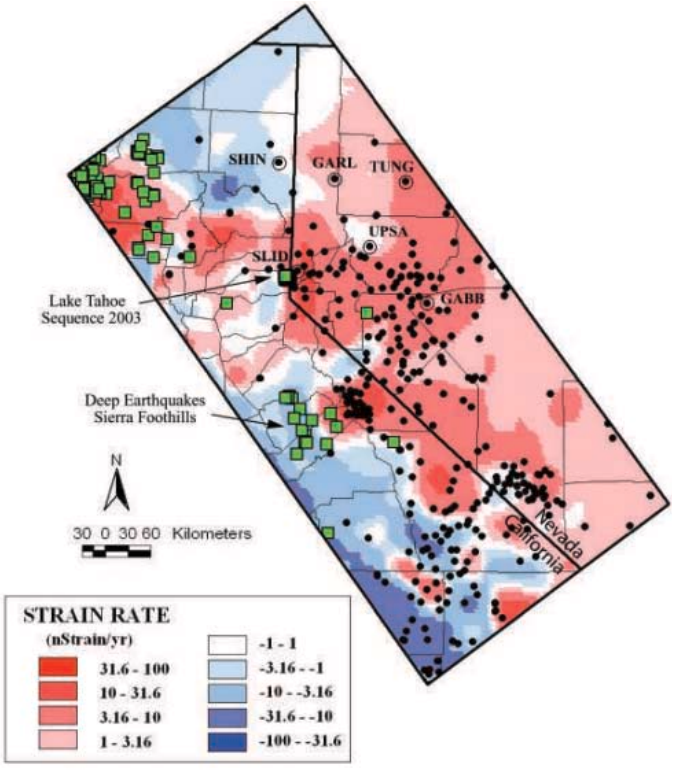

Fig. 4. Dilatational strain map determined from GPS stations in the Sierra Nevada region. Black circles are stations used in calculating dilatational strain in nanostrains per year (nstrain/yr) and circles within circles are BARGEN array stations. Best-located events from the Advanced National Seismic System (ANSS) earthquake catalog between depths of 20 and 50 km (green squares) are included.

error in SLID's displacement and are consistent to within 2 SD of the formal errors.

These results yield a transient change in velocity of SLID between July 2003 and January 2004 of 20 ± 2 mm/year (12 ± 1 mm/year horizontally). This in turn implies a lower bound on transient strain rates of ~200 nanostrains per year (120 nanostrains per year horizontally) in the region between SLID and neighboring stations. These rates are several times higher than (and in addition to) the 1996 to 2003 regional strain rate of 30 to 40 nanostrains per year reported from BARGEN observations before the transient event (*2*), and an order of magnitude greater than the estimated errors.

The extent of fault rupture is typically estimated from aftershock distributions. The area of the planar structure at depth (40 km^2), assuming a stress drop of 10 MPa (reasonable for upper-crustal earthquakes), would cause a seismic moment equivalent to an M_w of 6.0 and displacement of ~1 m at the source. Reverse faulting on the imaged structure at depth (hanging wall up and to the southwest) would result in horizontal displacements at SLID up and to the southwest, so the horizontal component would be in the opposite direction of the observations. Normal faulting, on the other hand, although characteristic of the Lake Tahoe region, would result in a loss of elevation at SLID. However, a dilatational mechanism can fit the geodetic data. Applying Okada's (*19*) model for a tensile crack at 30-km depth in the source region, a potency equivalent to a volume of 3.7×10^7 m^3, or a volumetric moment equivalent to M_w 6.1, fits the SLID observations (SOM text). Because only one GPS station is available, the source of the displacements at SLID cannot be uniquely determined. Mechanisms such as the introduction of fluids in the volume between the deep swarm and SLID or volumetric expansion of a potential source of magma below the deep-crustal swarm could be developed to fit SLID motions.

The temporal correlation of SLID motions and deep seismicity strongly suggests that the source of SLID displacements is spatially correlated with the earthquake swarm. SLID motions are not consistent with a shear dislocation but with dilatational or tensile failure, along the deep structure. Also, the progression of earthquake depths and stress field implied from earthquake focal mechanisms is consistent with other observations of dike intrusion (*8*). In addition, the high *b* value of

the Lake Tahoe sequence is most likely in response to rock failure due to a high strain rate, typical of dike injection (*7*). The injection front of a propagating dike is reflected by the temporal progression of earthquake depths, whereas the high-frequency character of the events requires brittle failure of rock at the crack tip. Also, tensile failure along east-dipping structures would be consistent with east-west extension along the Great Basin Sierra Nevada transition near Lake Tahoe. High dilatational strain rates are inferred from GPS data in the Lake Tahoe region (Fig. 4). SLID deformation and the character of the earthquake swarm are consistent with magma injection. The volumetric source required to fit SLID observations would correspond to a ~1-m-thick dike over the area of the imaged structure at depth. Dipping eastward at 50°, the lower-crustal structure would project to the surface west of the Sierra Nevada Great Basin frontal fault system west of Lake Tahoe. However, if a Sierra Nevada/Great Basin–bounding structure, or structural zone, shallows eastward into the lower crust, the event may have taken place near or within this structural boundary.

Periodic aseismic transient deformation in the Cascadia subduction zone is associated with deep-crustal LP earthquakes (25 to 45 km in depth) with tremor-like seismic signatures (*20*, *21*). Outside of subduction regions, however, deep brittle–failure earthquakes are uncommon because of the predominance of a brittle-ductile transition in the mid-crust and increased temperature with depth. Brittle failure at these depths requires localized high strain rates that can result from magma injection. Deep earthquakes observed in the western Sierra Nevada foothills (*22*) may be in response to the same mechanism (Fig. 4). We suggest that this magmatic phenomenon should not be viewed as a likely precursor to volcanism, but rather as part of the tectonic cycle of lower-crustal evolution, perhaps providing a mechanism to sustain crustal thickness and crustal strength in zones of extension.

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Powering Fuel Cells with CO via Aqueous Polyoxometalates and Gold Catalysts

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Electricity was produced by catalytic oxidation of carbon monoxide (CO) by using gold catalysts at room temperature. The observed rates are faster than conventional processes operating at 500 kelvin or higher for the conversion of CO with water to produce hydrogen and carbon dioxide through the water-gas shift (WGS). By eliminating the WGS reaction, we remove the need to transport and vaporize liquid water in the production of energy for portable applications. This process can use CO-containing gas streams from the catalytic reforming of hydrocarbons to produce an aqueous solution of reduced polyoxometalate compounds that can be used to generate power. The reduced polyoxometalate can be reoxidized in fuel cells that contain simple carbon anodes.

The production of H_2 for fuel cells typically involves the initial formation of a mixture of H_2, CO, and CO_2 from hydrocarbons or oxygenated hydrocarbons (*1–5*), followed by the water-gas shift (WGS) reaction ($CO + H_2O \rightarrow CO_2 + H_2$) to achieve the high conversions of CO to CO_2 (*6–9*) necessary for proton-exchange membrane (PEM) fuel cells, in view of the strong poisoning effects of CO on Pt-based anodes (*10*). The WGS reaction represents a major bottleneck in the production of H_2 because this exothermic reaction is slow at the low temperatures (~500 K) required to achieve favorable equilibrium conversions. In addition, the WGS reaction imposes an important limitation for the production of H_2 for portable applications because large amounts of liquid water must be transported and vaporized. Here, we demonstrate a process that bypasses the WGS reaction during the production of fuel-cell-grade H_2 by using the CO directly as an additional source of energy from H_2 streams. This process is especially promising for the production of electrical energy from renewable biomass-derived oxygenated hydrocarbons because these reactants have C:O stoichiometric ratios equal to 1:1, and they therefore generate H_2 and CO in nearly equal amounts during catalytic decomposition.

Our process for oxidation and use of CO involves the reaction of CO and liquid water with a reducible polyoxometalate (POM) compound, such as $H_3PMo_{12}O_{40}$, that serves as a strong oxidizing agent for CO and as an energy-storage agent for electrons and protons, over gold nanotubes or nanoparticles, and it takes advantage of the high catalytic activities of gold nanoparticles for CO oxidation (*11–13*), especially in the presence of liquid water (*14*, *15*). This catalytic process

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can be accomplished at room temperature, whereas the WGS reaction must be operated at elevated temperatures (at least 400 K and typically above 500 K) (*6*, *16*). In our process, CO is removed from the gas stream by oxidizing it to CO_2, thereby forming an aqueous solution of reduced POM species according to the following representative reaction:

$$CO_{(g)} + H_2O_{(l)} + PMo_{12}O_{40}^{3-}{}_{(aq)} \rightarrow CO_{2(g)} + 2H^{+}{}_{(aq)} + PMo_{12}O_{40}^{5-}{}_{(aq)}$$

This solution contains stored energy in the form of protons and electrons associated with reduced metal cations that can be reoxidized readily at a fuel-cell anode by the transfer of electrons from the POM to the electrode and the transport of protons through the PEM to the cathode. Accordingly, this process for CO oxidation not only removes CO from gas streams for fuel cells, but also converts the energy content of CO into a liquid that can subsequently be used to power a fuel cell. Thus, whereas previous studies of CO oxidation have used irreversible oxidizing agents such as O_2 (*17*, *18*), our process uses aqueous-phase POM compounds that undergo reversible oxidation-reduction reactions. In this way, the reducible POM compound facilitates the CO removal step by undergoing reduction, and the reduced POM then serves as a fuel for the electrical energy generation step by undergoing oxidation at a fuel-cell anode. Thus, the use of the POM species as redox shuttle eliminates the need to convert CO with H_2O to gaseous H_2 and CO_2 as an intermediate reaction for power generation.

To illustrate a possible application of our process for CO use, we consider ethylene glycol as a fuel source, which decomposes according to the stoichiometric reaction

$$C_2O_2H_{6(l)} \longrightarrow 2CO_{(g)} + 3H_{2(g)}$$

This reaction can be carried out by using a supported catalyst (for example, 3 weight percent Pt/Al_2O_3) with CO and H_2 selectivities of 90% or greater with 50% conversion of ethylene glycol at the temperatures near 500 K. Ethylene glycol dissociation is endothermic (234 kJ mol^{-1}) and requires combustion of 0.83 moles of CO for an energetically neutral process to produce 3 moles of H_2 and 1.17 moles of CO for energy production. If the H_2 and CO are separated, then the H_2 can be sent to a PEM fuel cell operating at 50% efficiency, 0.83 moles of CO can be combusted, and the remaining 1.17 moles of CO can be converted to electrical energy at 0.35 V (corresponding to ~25% of the standard Gibbs free-energy change for CO combustion). The overall efficiency for production of energy from the ethylene glycol fuel by this process is equal to 40%. This process does not require the use of water, as would be needed for ethylene glycol reforming (*2*, *3*).

$$C_2O_2H_{6(l)} + 2H_2O_{(l)} \longrightarrow 2CO_{2(g)} + 5H_{2(g)}$$

In this respect, the energy content of liquid ethylene glycol is about 20 kJ cm^{-3} (equal to 60% of the value for octane), whereas the energy content of a stoichiometric liquid mixture of ethylene glycol and water is about 10 kJ cm^{-3}. In contrast, the energy density of H_2 at a pressure of 690 bar (~10,000 psi) is only equal to about 7.5 kJ cm^{-3}. Moreover, the ethylene glycol fuel is nonflammable and can be stored safely.

Figure 1 shows a schematic representation of the reactor system used to study the reduction of aqueous solutions of POM compounds by CO in a gold nanotube membrane reactor and the subsequent generation of electrical energy from these reduced POM solutions that contain protons in the aqueous phase and electrons associated with the POM. Most of our studies were carried out using aqueous solutions of $H_3PMo_{12}O_{40}$ [which has the Keggin structure comprised of tetrahedral PO_4 surrounded by 12 octahedral MoO_6 (*19*)] as the POM oxidizing agent, which is yellow in color and stable at temperatures up to 473 K in solid form. Reaction with CO over the gold catalyst leads to the formation of CO_2 and an aqueous solution that has the characteristic deep blue color that is caused by charge transfer between Mo^{5+} and neighboring Mo^{6+} species (*20*). The reduction of $H_3PMo_{12}O_{40}$ by CO does not take place at room temperature without the gold catalyst. This aqueous solution containing reduced POM species was delivered to a fuel cell constructed with an anode fashioned from a gold nanotube membrane or made from a simple carbonlike graphite without any precious metal. The cathode of the fuel cell was comprised of Pt supported on carbon for cases in which O_2 was used as the oxidizing agent (the upper fuel cell system in Fig. 1). For cases in which the oxidizing agent was an aqueous solution of $H_3PMo_{12}O_{40}$, the cathode was composed of a gold nanotube membrane or made from carbon (the lower fuel cell system in the figure). The latter case is a completely precious metal–free fuel-cell system. Oxidation of the reduced POM solution at anode does not require a precious-metal electrode because the protons and electrons have already been separated during the CO oxidation step over the gold catalyst.

The rate of CO_2 production (Fig. 2) with aqueous solutions of POM compounds on gold nanotube membranes increases with the concentration of the aqueous POM solution up to 0.05 M, and the rate is first order with respect to the partial pressure of CO in the gas stream. [Images of gold nanotubes from scanning electron microscopy are presented

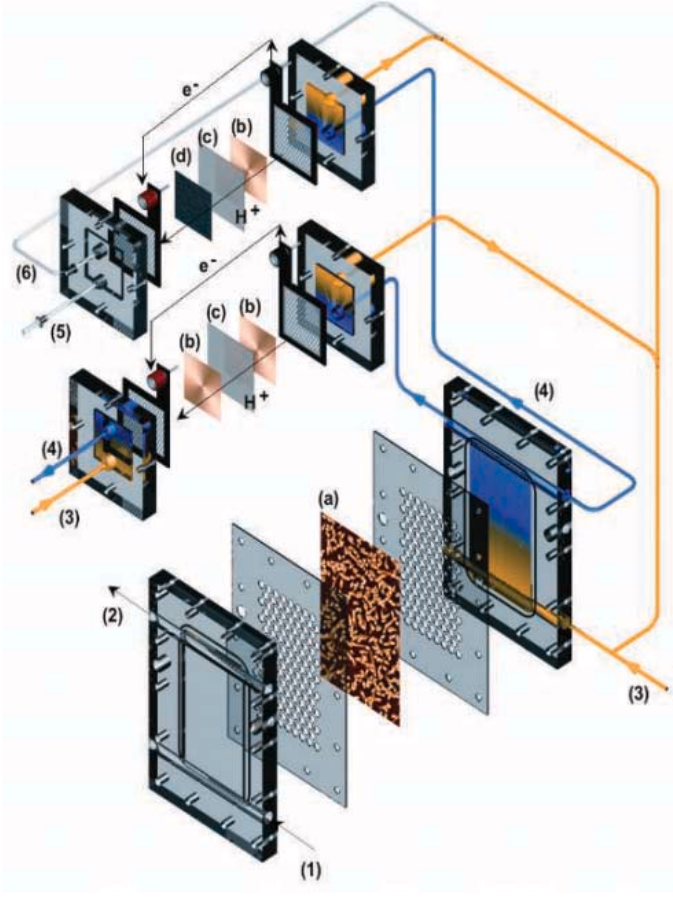

Fig. 1. Schematic diagram of the membrane reactor coupled with fuel cells to study CO oxidation at the membrane reactor and energy transfer at the fuel cells. (1) CO inlet, (2) CO_2 outlet, (3) oxidized POM inlet, (4) reduced POM outlet from membrane reactor and from fuel cell cathode or inlet to the fuel cell anodes, (5) O_2 inlet, (6) H_2O outlet, (a) gold nanotube membrane catalyst after RIE for the interface of CO gas and liquid POM solution, (b) electrodes fashioned from a simple carbon or gold nanotube membrane with surface gold, (c) Nafion PEM, and (d) cathode made of Pt/C.

in fig. S1 (*21*).] The rate is enhanced when the gold nanotubes within the track-etched pores of polycarbonate template were exposed from the polycarbonate to a depth of 1 to 2 μm by selectively etching the membrane using reactive ion etching (RIE) with an O_2 plasma (*22*). The rate of CO oxidation per gram of gold is greater for membranes containing smaller amounts of gold because the average particle size of gold is smaller for these materials (fig. S1), thus leading to higher surface areas per gram of gold. This result suggests that the rate of CO oxidation can be altered by changing the morphology of the gold catalyst, for example, by changing the inner and/or outer pore diameters of the gold nanotubes.

Catalysts consisting of gold nanoparticles on various supports should be promising candidates for achieving high rates of CO oxidation by aqueous solutions of POM compounds, because these catalysts have been shown to exhibit high rates of CO oxidation by O_2 (*17*, *18*) or by H_2O (*6*, *23*) at low temperatures. Indeed, we have observed very high rates of CO oxidation by aqueous solutions of $H_3PMo_{12}O_{40}$ over nanoparticles of gold supported on carbon or titania with gold catalysts provided by the World Gold Council (sample 4D or 18A, respectively) (fig. S2). Typically, these experiments were carried out at 298 K in a pressurized batch reactor at a CO pressure of 15 bar with 20 cm^3 of 0.05 M POM solution. The rate of CO_2 production at low conversions was approximately 16×10^4 μmol gAu^{-1} min^{-1} (~3500 cm^3 at 273 K and 1 bar of gaseous CO_2 produced per gram of gold per minute), which is equivalent to a turnover frequency (TOF) of 4.3 s^{-1}, assuming a gold dispersion of 12% based on the average diameter of the gold particles (7 to 10 nm) on carbon. This high specific rate achieved even at room temperature is comparable to or even faster than rates of CO oxidation by O_2 over supported gold catalysts at 353 K (30×10^4 μmol gAu^{-1} min^{-1}) (*24*) and rates of WGS over cyanide-leached gold catalysts at 523 K (3.7×10^4 μmol gAu^{-1} min^{-1}) (*6*). The rate of CO_2 production and TOF are very high at pressures near 1 bar (equal to 3×10^4 μmol gAu^{-1} min^{-1} and 0.85 s^{-1}, respectively, as shown in fig. S2), which suggests that our room-temperature process could be applied to gaseous streams produced from a conventional catalytic reforming of hydrocarbons, without involving the WGS reaction as an intermediate step to remove CO. Moreover, we have observed that the rate of CO oxidation by our process is 10 times as fast as the rate of H_2 oxidation when both gases are passed separately over a gold catalyst, and the rate of CO oxidation is at least an order of magnitude faster than the rate of H_2 oxidation when using a $CO:H_2$ gas mixture containing 10% CO. The rate of H_2 oxidation was measured by monitoring the color change of the POM solution using an ultraviolet-visible spectrometer operating at 500 nm. These results indicate that our process can be used to effectively remove CO from H_2 gas streams for fuel-cell applications.

The highest energy density obtained in this work was 2.5 moles of CO_2 produced per liter of solution containing $H_3PMo_{12}O_{40}$ at a concentration of 1 M, corresponding to 5 electrons per Keggin unit. This extent of storage was achieved with a pressurized batch reactor containing the solution of POM compound with gold nanoparticle catalysts, operating at room temperature and a CO pressure of 15 bar. The extent of POM reduction calculated from the CO_2 production agreed within 20% with the extent of reduction measured by integrating the electrical current versus time produced when the reduced solution was completely reoxidized in a fuel cell discharged at constant resistance, and dividing this value by the Faraday constant. [See table S1 for details (*21*).] We believe that the rate of CO oxidation as well as the energy storage capacity could be improved by further studies among the large number of other POM compounds that can be synthesized (*25*).

The generation of power by using reduced POM solutions, produced from CO oxidation, is not limited to conventional electrodes (e.g., Pt based). Figure 3 shows curves of voltage versus current density from a single cell for various combinations of anodes, cathodes, and reduced POM solutions. Although higher current densities (by 20 to 50%) are achieved with electrodes containing precious metals (i.e., Pt, Au) with a Nafion (Sigma-Aldrich, St. Louis, MO, USA) PEM (*21*), it can be seen that good current densities can be generated with a simple carbon anode. Good current densities can be generated even when the Pt-containing cathode used with O_2 is replaced by a simple carbon cathode used with oxidized $H_3PMo_{12}O_{40}$.

Current H_2 PEM fuel cells operating with Pt-based electrodes have current densities higher than 100 mA cm^{-2}. However, these fuel cells have been highly optimized, and they require precious metals to oxidize H_2 at the anode and reduce O_2 at the cathode. Our

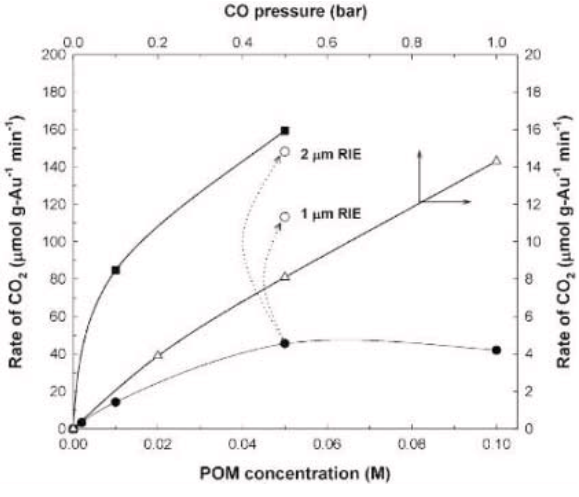

Fig. 2. Rate of CO oxidation with POM ($H_3PMo_{12}O_{40}$) on gold nanotube membranes at 298 K and a total pressure of 1 bar. Rate of CO_2 production on membrane prepared by electroless deposition of gold for 2 hours versus POM concentration (filled circles), versus CO partial pressures (M = 0.01) (open triangles), and after RIE treatment to remove 1 and 2 μm of membrane. Rates also shown on membrane prepared by electroless deposition of gold for 0.25 hours versus POM concentration (filled squares).

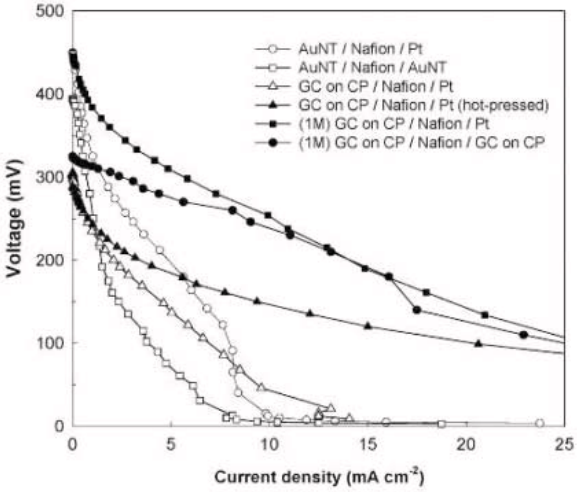

Fig. 3. Voltage-current curves on the various combinations of anodes, membranes, and cathodes with reduced $H_3PMo_{12}O_{40}$ solution used as fuel. As an oxidant, O_2 was used for the Pt cathode and oxidized $H_3PMo_{12}O_{40}$ was used for gold or carbon cathodes. All curves were obtained with 0.5 M $H_3PMo_{12}O_{40}$, except the filled squares and filled circles with 1 M solution. AuNT, gold nanotube membrane deposited for 2 hours with surface gold; Pt, Pt/C cathode; GC, graphitic carbon; CP, carbon paper.

studies demonstrate the feasibility of making new generations of inexpensive fuel cells that operate with solutions of reduced POM compounds and that have current densities of at least 10 mA cm^{-2}. This current density was increased by a factor of 3 at 100 mV and by a factor of 4 or greater at 50 to 100 mV when the assembly consisting of carbon anode, Nafion, and Pt cathode was treated by hot-pressing at 400 K, as included in Fig. 3 (compare open versus filled triangle symbols). Thus, we believe that further optimization with these new fuel cells will lead to improved current densities and improved utilization of precious metals at the electrodes.

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Plasminogen Is a Critical Host Pathogenicity Factor for Group A Streptococcal Infection

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Group A streptococci, a common human pathogen, secrete streptokinase, which activates the host's blood clot–dissolving protein, plasminogen. Streptokinase is highly specific for human plasminogen, exhibiting little or no activity against other mammalian species, including mouse. Here, a transgene expressing human plasminogen markedly increased mortality in mice infected with streptococci, and this susceptibility was dependent on bacterial streptokinase expression. Thus, streptokinase is a key pathogenicity factor and the primary determinant of host species specificity for group A streptococcal infection. In addition, local fibrin clot formation may be implicated in host defense against microbial pathogens.

Plasmin, the major serine protease that degrades the fibrin blood clot, is generated through cleavage of the proenzyme plasminogen (PLG) by the plasminogen activators urokinase (uPA) and tissue-type plasminogen activator (tPA). Human PLG can also be activated by streptokinase (SK) secreted by group A streptococci (GAS), leading to the clinical use of SK for therapeutic fibrinolysis of pathologic thrombi associated with myocardial infarction, stroke, and venous thrombosis (*1*). PLG deficiency results in the rare genetic disorder ligneous conjunctivitis, characterized by thick fibrinous pseudomembranous deposits on the conjunctiva and other mucous membranes (*2*). PLG null mice develop spontaneous fibrin deposition in multiple tissues, leading to retarded growth, rectal prolapse, and decreased survival (*3*, *4*). *Plg* null mice also exhibit eye findings similar to those for the human disease (*5*). In addition to GAS, a number of other human pathogens also express a plasminogen activator, including staphylokinase of *Staphylococcus aureus* (*6*) and the Pla protein of *Yersinia pestis*, the agent responsible for the plague (*7*). Other microbes, such as *Borrelia burgdorferi*, use a host plasminogen activator as a pathogenicity factor (*8*, *9*). GAS is the most common cause of clinically significant bacterial pharyngeal and skin infections. A subset of these infections are highly invasive into soft tissues or organs and result in rapidly progressive, life-threatening conditions, such as necrotizing fasciitis (*10*). Like many microbial pathogens, GAS is highly host-specific and naturally only infects humans. This restricted host specificity is correlated with the limited ability of many candidate pathogenicity factors, including SK and surface receptors for PLG, to interact with ligands or protein substrates from species other than humans (*11*–*16*). Studies of streptococcal pathogenicity and the role of SK and surface-bound PLG-binding proteins have been hampered by this limitation, as well as by species-specificity in the interactions among host fibrinolytic system components, including tPA and PLG (*17*).

We generated a "humanized" transgenic mouse expressing human PLG under control of the mouse albumin gene regulatory sequences within a bacteria artificial chromosome (BAC) transgene [(*18*) and fig. S1A]. Two independent founder lines, *AlbPLG1* and *AlbPLG2*, directed highly liver-specific *PLG* expression (fig. S1B). The level of PLG detected in the plasma of *AlbPLG1* corresponded to ~17% of the PLG level in control human plasma (16.7 ± 1.78) with a much lower level (<1%) for *AlbPGL2*. Consistent with previous reports (*11*, *15*), human PLG derived from the transgene also exhibited increased susceptibility to activation by human tPA and SK compared with mouse PLG (fig. S1, C and D) (*17*, *19*).

Mice that are $Plg^{-/-}$ are viable but exhibit

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retarded growth, diffuse fibrin deposition in multiple tissues, and frequent rectal prolapse (*3*, *4*). Introduction of the human PLG transgene resulted in reversal of the widespread tissue fibrin deposition observed in the livers of $Plg^{-/-}$ mice and near-complete rescue of the weight loss and rectal prolapse phenotypes (Fig. 1, A to D, and fig. S2). The fibrinolytic system is thought to play a critical role in controlling the thrombotic complications associated with bacterial sepsis (*20*), and mice deficient in α2-antiplasmin exhibit enhanced fibrin clearance after endotoxin [lipopolysaccharide (LPS)] administration (*21*). We also tested the response of $Plg^{-/-}$ mice to LPS (Fig. 1E). Here too, human PLG directed by the *AlbPLG1* transgene could substitute for the orthologous mouse protein and rescued the $Plg^{-/-}$ mice from markedly reduced survival.

Mice are generally highly resistant to skin infection by most human pathogenic GAS, with intradermal injection of 10^8 CFU of one such strain resulting in only ~20% mortality at 6 days in outbred CD1 mice (*19*). The GAS strain UMAA2616 exhibits enhanced virulence in a mouse skin infection model because of site-directed mutation in the regulatory locus, *csrRS* (*22*). Using this strain at a dose of 2×10^5 CFU, we observed 20% mortality at 9 days in control littermate mice on the C57BL/6J background. However, introduction of human PLG expressed by the *AlbPLG1* transgene markedly increased mortality to 75% (Fig. 2A). MGAS166, the wild-type clinical isolate from which the hypervirulent UMAA2616 strain was derived, caused no mortality at 10 days in control mice injected with up to 7×10^6 CFU and only 30% mortality at 7 days after a dose of 3×10^7 CFU. Corresponding mortalities in Tg^+ mice ranged from 35 to 100% (Fig. 2, B to D). Thus, human PLG plays a critical role in the pathogenicity of these human GAS isolates in this mouse model, a function that is not provided by mouse PLG. The *AlbPLG2* transgene directs only very low levels of human PLG expression (<1%). Although a trend to increased mortality was seen in animals carrying the *AlbPLG2* transgene, this effect was not statistically significant (Fig. 2E). Thus, there appears to be a minimal threshold level of human PLG that is required for GAS pathogenicity.

Enhanced virulence is observed in GAS skin infection in the mouse after preincubation with human plasma or coinjection with purified human PLG (*14*). Increased invasiveness is also seen when GAS is preincubated with SK and human fibrinogen and PLG in vitro (*19*). Species specificity has also been demonstrated for PLG receptors on the bacterial surface and for interactions with fibrinogen (*11-13*, *15*). To test the relative contribution of SK to the overall host species specificity of human pathogenic streptococci, we inoculated animals with an isogenic streptococcal strain deleted for the SK gene (*ska*, UMAA2641) (*14*). The increased susceptibility of Tg^+ mice to the wild-type GAS isolate UMAA2616 was largely abrogated by deletion of *ska*. The 75% mortality observed at 9

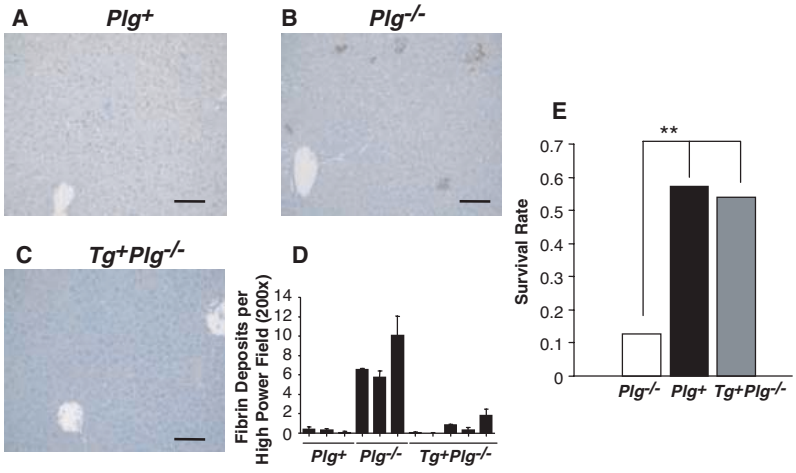

Fig. 1. Rescue of $Plg^{-/-}$ phenotype by human *PLG* transgene. (**A** to **C**) Liver sections immunostained for fibrin(ogen). Scale bar, 100 μM. (**D**) Hepatic deposits of fibrin(ogen) per high power field (200×) were quantified by blinded analysis of liver samples from three Plg^+ ($Plg^{+/+}$ or $Plg^{+/-}$), three $Plg^{-/-}$, and five $Tg^+Plg^{-/-}$ mice at 10 weeks of age. (**E**) Survival rate of Plg^+, $Plg^{-/-}$, and $Tg^+Plg^{-/-}$ mice 3 days after intraperitoneal injection of 13.5 μg LPS per gram body weight. $^{**}P < 3 \times 10^{-5}$.

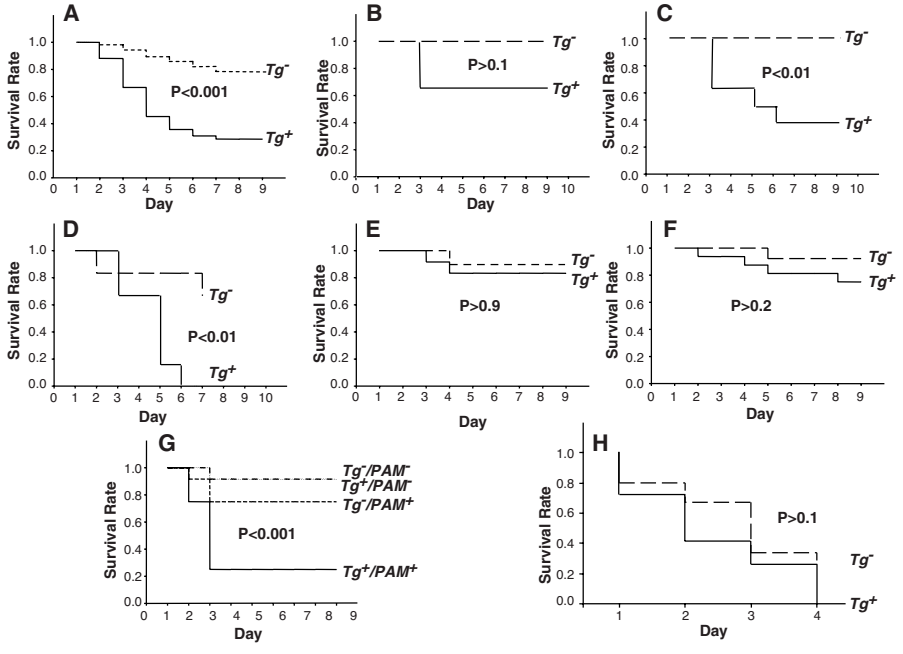

Fig. 2. Increased susceptibility to GAS conferred by human PLG. Survival curves for Tg^- mice are indicated by dashed lines and for Tg^+ mice by solid lines. *P* values were determined by log-rank test. (**A**) Survival curve of *AlbPLG1*Tg^- and Tg^+ mice after infection with 2×10^5 CFU UMAA2616. Data are pooled from five independent injections with at least five mice per group for each experiment (a total of 42 Tg^+ and 56 Tg^- mice). (**B** to **D**) Survival curve of Tg^- and Tg^+ mice after inoculation with strain MGAS166 at three different doses, 3×10^5, 7×10^6, and 3×10^7 CFU. Each group contains at least six mice. (**E**) Survival curve of *AlbPLG2* Tg^- and Tg^+ mice after inoculation with 2×10^5 CFU UMAA2616. Data are pooled from two independent experiments. Each group consisted of 6 to 10 mice (a total of 16 Tg^+ mice and 13 Tg^- mice). (**F**) Survival curve of *AlbPLG1* Tg^- and Tg^+ mice after inoculation with the SK-deficient strain 2×10^5 CFU UMAA2641. Data are pooled from two independent experiments. Each group consisted of 4 to 6 mice (a total of 12 Tg^+ mice and 10 Tg^- mice). (**G**) Survival curves of *AlbPLG1* Tg^- and Tg^+ mice after subcutaneous injection with the 10^8 CFU PAM-expressing strain AP53 and an isogenic derivative of the AP53 strain deficient in PAM expression. Data are pooled from two independent experiments (with a total of 12 mice in each group). (**H**) Survival curves of *AlbPLG1*Tg^- and Tg^+ mice after infection intravenously with 2×10^6 CFU UMAA2616. Data are pooled from three independent experiments with 5 mice per group for each experiment (a total of 15 Tg^+ and 15 Tg^- mice).

days with strain UMAA2616 (Fig. 2A) contrasted with the 27% mortality using its *ska*-deleted derivative (Fig. 2F). Although not statistically significant ($P > 0.2$), a trend toward increased mortality in Tg^+ mice infected with the SK^- strain compared with their Tg^- littermate controls is consistent with an additional contribution of other host species–specific PLG-dependent factors.

We next examined the potential role of the bacterial surface protein (PAM) that is expressed by a subset of GAS associated with skin infections. PAM specifically binds human PLG or plasmin with high affinity, although exhibiting considerably weaker binding to mouse PLG (*12*). The PAM-expressing GAS strain AP53 produced low levels of SK and exhibited low virulence in Tg^- mice (~20% mortality) (Fig. 2G). In contrast, Tg^+ mice were much more susceptible to the AP53 strain, with mortality increased to ~80%. An isogenic derivative of the AP53 strain deficient in PAM expression, and thus unable to bind PLG, showed minimal virulence in both Tg^+ and wild-type mice, which suggested that the amount of SK secreted by this strain was not sufficient to allow bacterial dissemination in the absence of PAM. Thus, the ability to focus PLG at the bacterial surface provides an additional mechanism whereby GAS, and potentially other pathogens, can exploit the host fibrinolytic system to facilitate establishment of infection and subsequent invasion.

A number of mechanisms have been proposed to explain how the recruitment and activation of PLG by an invasive bacterial pathogen might enhance virulence (*16*). It is likely that the host inflammatory response to bacterial infection results in local thrombosis and microvascular occlusion. This response may serve to seal off the infectious nidus and to prevent systemic spread. We hypothesized that GAS hijacks the host fibrinolytic system in order to circumvent this local defense and to reopen the vascular tree to systemic spread. Consistent with this model, we observed an increase in bacterial colonies in the spleens of Tg^+ mice injected with 2 to 3 $\times$ 10^7 CFU MGAS166 (Fig. 3A) or 10^8 CFU AP53 (Fig. 3B) compared with Tg^- controls, presumably representing increased systemic spread. This enhanced dissemination may also explain the observed increase in mortality in these animals (Fig. 2. A to D, and G).

If GAS-associated fibrinolysis is required primarily to facilitate bacterial access to the vasculature, then pathogenic GAS introduced via the intravenous route should no longer depend on human PLG function. Indeed, no difference in mortality was observed between Tg^+ and Tg^- mice injected intravenously with 2 $\times$ 10^6 CFU of UMAA2616 (Fig. 2H), in contrast to the marked difference in mortalities seen when the same genotypes were injected subcutaneously (Fig. 2A).

Although these data suggest that GAS-induced PLG activation is required to overcome local microvascular occlusion, we observed no difference in bacterial colony counts from homogenized local skin lesions (Fig. 3A), and histological analysis of skin surrounding the inoculation site failed to identify an obvious difference in fibrin deposition or vascular occlusion between Tg^+ and Tg^- animals (Fig. 3C and fig. S2C). Thus, bacterial-induced fibrin dissolution may be transient, or localized to specific invasive sites, and not evident on gross histologic examination.

To further explore the role of fibrin deposition in host defense against the dissemination of SK-expressing streptococcal pathogens, we examined mortality after GAS injection in C57BL/6J mice treated with the snake venom Ancrod, which proteolytically degrades plasma fibrinogen (*23*). Ancrod-treated animals demonstrated an approximately 60% reduction in plasma fibrinogen. This decrease in fibrinogen was also associated with a marked increase in mortality after a subcutaneous inoculum of 9 $\times$ 10^6 CFU MGAS166, from 30% at 6 days in control animals to 100% in Ancrod-treated mice (Fig. 3D).

Thus, activation of host PLG by SK leads to accelerated clearance of host fibrin and is a central mechanism for GAS invasion and spread. It is likely that similar interactions are central to the invasive program of other unrelated, plasminogen activator–associated pathogens that occupy diverse microenvironmental niches, such as *S. aureus*, *B. burgdorferi*, and *Y. pestis* (*6*–*9*). The remarkable species specificity of SK for host PLG probably resulted from host and pathogen coevolution (*15*). Similar coevolution probably also explains the recently reported specificity of the *Neisseria meningitides* for human CD46 (*24*).

Our findings raise the possibility that polymorphic variation in the level of plas-

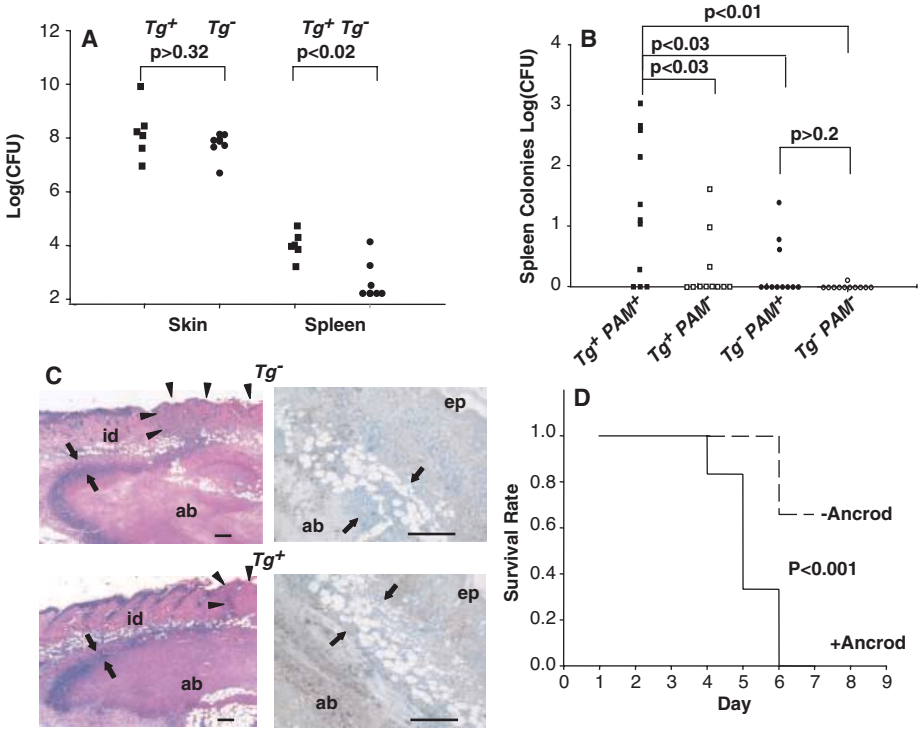

Fig. 3. Fibrin as a barrier to GAS dissemination. (**A**) Spleen and skin lesions were harvested at 64 hours and bacterial colonies quantified. Each data point represents one mouse. Although potentially partially masked by increased mortality in Tg^+ mice, a significant difference in mean bacterial colonies (CFU) in the spleen was still observed between Tg^+ (■) and Tg^- (●) mice (*P* values determined by Mann-Whitney test). (**B**) Similar data were obtained for Tg^- (circles) and Tg^+ (squares) mice infected with strain AP53 (filled symbols) or the isogenic PAM^- mutant (open symbols). Spleens were dissected after 24 hours, and the number of CFUs was determined. Enhanced splenic spread is observed in Tg^+ mice infected with the PAM^+ strain compared with the PAM^- strain. Greater levels of spread were also observed in Tg^+ mice compared with Tg^- mice for both the PAM^+ and PAM^- strains (*P* values determined by Mann-Whitney test). (**C**) Representative hematoxylin and eosin–stained sections (left) from the injection site, 64 hours after inoculation with 2 to 3 $\times$ 10^7 CFU UGAS166. An acutely inflamed dermis (id) is evident, along with about half of a bacteria-induced abscess (ab) surrounded by a rimlike infiltrate of neutrophils (arrows), and with acute inflammation and central necrosis of the overlying epidermis (ep) (outlined with arrowheads) in both Tg^+ and Tg^- mice. Scale bar: 100 μM. (**D**) Survival curve of Ancrod-treated (solid line) and control mice (dashed line) after injection with 9 $\times$ 10^6 CFU of strain MGAS166 (six mice per group).

minogen, and potentially other fibrinolytic components, within human populations could represent a significant susceptibility factor for bacterial infection. Another virulence determinant was recently shown to form complexes with fibrinogen that induce vascular leakage, potentially enhancing the severity of GAS infection (*25*). These observations highlight the potential role of infectious disease as a critical force in the evolution of the hemostatic system and the unusual species specificity of many coagulation factor interactions.

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E Protein Silencing by the Leukemogenic AML1-ETO Fusion Protein

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The AML1-ETO fusion protein, generated by the t(8;21) chromosomal translocation, is causally involved in nearly 15% of acute myeloid leukemia (AML) cases. This study shows that AML1-ETO, as well as ETO, inhibits transcriptional activation by E proteins through stable interactions that preclude recruitment of p300/CREB-binding protein (CBP) coactivators. These interactions are mediated by a conserved ETO TAF4 homology domain and a 17–amino acid p300/CBP and ETO target motif within AD1 activation domains of E proteins. In t(8;21) leukemic cells, very stable interactions between AML1-ETO and E proteins underlie a t(8;21) translocation-specific silencing of E protein function through an aberrant cofactor exchange mechanism. These studies identify E proteins as AML1-ETO targets whose dysregulation may be important for t(8;21) leukemogenesis, as well as an E protein silencing mechanism that is distinct from that associated with differentiation-inhibitory proteins.

The t(8;21) chromosomal translocation fuses an N-terminal region of the AML1 transcription factor to a nearly complete ETO protein and is one of the most frequent chromosomal abnormalities seen in both childhood and adult acute myeloid leukemia (AML) (fig. S1) (*1*, *2*). ETO and *Drosophila* Nervy share four highly similar Nervy homology regions (NHR1, -2, -3, and -4). Both ETO and AML1-ETO associate with histone deacetylase (HDAC) complexes and, independently, form high–molecular-weight nuclear oligomers (*3*). The NHR1 region (also known as the TAF4 homology or TAFH domain) also displays significant homology with a conserved region of TBP-associated factor 4 (TAF4) proteins (fig. S1) that reside within the TFIID transcription factor (*1*, *2*).

Mass spectrometric analyses of anti-FLAG immunoprecipitates from nuclear extracts of FLAG-ETO–expressing HeLa cells identified two predominant ETO-interacting polypeptides (Fig. 1A, left), whose identities were determined to be MTGR1 (*4*), an ETO dimerization partner, and the basic helix-loop-helix (bHLH) transcription factor HEB (HeLa E-box–binding protein), a member of the E protein family that also includes E2A and E2-2 (*5*, *6*). Western blots revealed additional ETO associations with the E protein E2A and, consistent with published results (*3*), with multiple components of HDAC complexes (Fig. 1A, right). Analyses of FLAG-HEB immunoprecipitates (from transfected cells) revealed extremely stable ETO-HEB associations (resistant to up to 1 M NaCl and high concentrations of detergents) and further indicated that HEB directly interacts with ETO (or with AML1-ETO) in a stoichiometric manner (fig. S2, A and B).

Ectopic expression of ETO or AML1-ETO completely abolished transactivation by a Gal4-HEB fusion protein and, further, converted it to a potent repressor, whereas it only minimally affected the baseline transcription observed with Gal4-DBD (Fig. 1B) or transactivation observed with Gal4-VP16 or liganded Gal4-TR (fig. S2C). In further analyses with an E-box–containing template, ectopic ETO similarly abrogated transactivation by HEB (Fig. 1C, lane 2 versus lane 3) in a dose-dependent manner (fig. S3B). Next, we determined that an ETO TAFH (eTAFH) domain (fig. S3A) is both necessary and sufficient for inhibiting HEB-dependent transcription. Thus, removal of eTAFH domain residues 93 to 189 (Fig. 1C), but not other regions such as NHR2 (Fig. 1C), NHR3, and ZnF (fig. S3, A and B), completely abolished the inhibitory effect. Furthermore, the eTAFH domain alone (Fig. 1C), with a critical requirement for subregions 93 to 109 and 152 to 179 (fig. S3, A and B), showed a potent inhibition of HEB transcription, although to a lower magnitude than that effected by full-length ETO (see also figs. S3B and S4E). This suggests contributions from other ETO regions to total inhibition of HEB function. Consistent with their ability to inhibit HEB-dependent transcription, ectopic ETO and AML1-ETO, but not the eTAFH-deleted ETO mutant (ETOΔeTAFH), strongly interacted with HEB in vivo (Fig. 1D). Further analyses documented direct eTAFH-HEB inter-

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actions in solution (fig. S3C) and on an E-box element both in vitro (Fig. 1E) and in vivo (fig. S3D). Together, these results establish the eTAFH domain as the ETO region that interacts with HEB. Ectopic ETO and AML1-ETO similarly selectively target and inhibit activation by E proteins E2A and E2-2 [fig. S4, A to C, and (*7*)]. Moreover, consistent with a requirement for ubiquitous E proteins as cofactors for tissue-specific (class B) bHLH transcription factors such as MyoD (*8*), ETO markedly inhibited MyoD-dependent transactivation (fig. S4D). This inhibition requires both the eTAFH domain (fig. S4D) and another ETO region or regions (fig. S4E) that presumably help to overcome the MyoD activation domain through recruitment of HDAC complexes.

E proteins contain two conserved activation domains (an N-terminal AD1 and a central AD2) and a C-terminal bHLH-type DNA binding domain. We next determined that ETO selectively targets the AD1 activation domain. First, the AD1 domain of either HEB (residues 1 to 99) or E2A, as a Gal4 fusion, is sufficient both for activation and for ETO-targeted inhibition (Fig. 2A and fig. S5D). Second, whereas ectopic ETO effected a marked dose-dependent repression of AD1-mediated transcription, it minimally affected transcription (possibly attributed to AD2) associated with the AD1-deleted HEB mutant (ΔAD1, residues 100 to 682) (Fig. 2B). In accordance, ETO failed to interact with the ΔAD1 protein in vivo while showing a strong interaction with full-length HEB (Fig. 2C). Finally, the ETO-HEB interaction was recapitulated in solution with the two defined interaction domains eTAFH and AD1 (fig. S4F).

An alignment of E protein AD1 domains (fig. S5A) reveals a highly conserved region (corresponding to residues 11 to 27 of HEB) characteristic of LXXLL-containing (L, Leu; X, any amino acid) amphipathic helices implicated in protein-protein interactions (*9*). Indicative of a requirement of this region for both ETO interaction and transactivation by AD1, a single $Leu^{17}\rightarrow Ala^{17}$ (L17A) point mutation (fig. S5C) disrupted both physical (Fig. 2D, top) and functional (Fig. 2D, bottom; see also figure legend) interactions of AD1 with ETO, as well as AD1-elicited activation (Fig. 2D, bottom). A proteomic search for polypeptides differentially bound to AD1, but not to inactive AD1-L17A, identified p300 and CREB-binding protein (CBP) histone acetyl transferases (HATs) as major cofactors for AD1 (fig. S6A). Thus, AD1 but not the L17A mutant interacts specifically with p300 and CBP, but not with other factors such as GCN5, TFIID (monitored by TAF4 and TBP), and TFIIE (fig. S6B). Analyses of truncated AD1 derivatives revealed that the conserved 17-residue fragment, HEB(11-27), is sufficient both for activation and for ETO-dependent silencing (Fig. 3A). In accordance, HEB(11-27) displayed strong selective interactions both with p300/CBP and with ETO or eTAFH (Fig. 3B). We thus designated this motif as PCET (p300/CBP and ETO target in E proteins). The lack of PCET interactions with N- and C-terminal truncated eTAFH explains the inability of these mutants to inhibit HEB activation (Fig. 3B and fig. S3, A and B). Consistent with an essential role of PCET in mediating p300/CBP recruitment, further analyses of transfected components showed that AD1 is required for HEB association both with a HAT activity and with endogenous p300 in 293T cells (Fig. 3C, lanes 1, 2, and 4).

We next determined that ETO interaction with HEB through its eTAFH domain blocks p300/CBP recruitment by HEB. Thus, coexpression of ETO dramatically lowered the levels of both p300 and the HAT activity associated with ectopic FLAG-HEB in 293T cells (Fig. 3C, lane 2 versus lane 3). In accordance, neither p300 nor HAT activity was found to associate with FLAG-ETO–bound HEB protein (fig. S5B). Moreover, an in vitro analysis showed that eTAFH formed a stoichiometric complex with HEB and dramatically inhibited HEB interactions with p300/CBP but not with TFIID (Fig. 3D, lane 2 versus lane 3). Along with the observation that TFIID does not interact detectably with AD1 (fig. S6B), this indicates that HEB may independently recruit both p300/CBP HAT cofactors and TFIID components through distinct domains. Further analyses of PCET (fig. S5, C to E, and Fig. 3E) showed that whereas hydrophobic residues (green), such as the L17

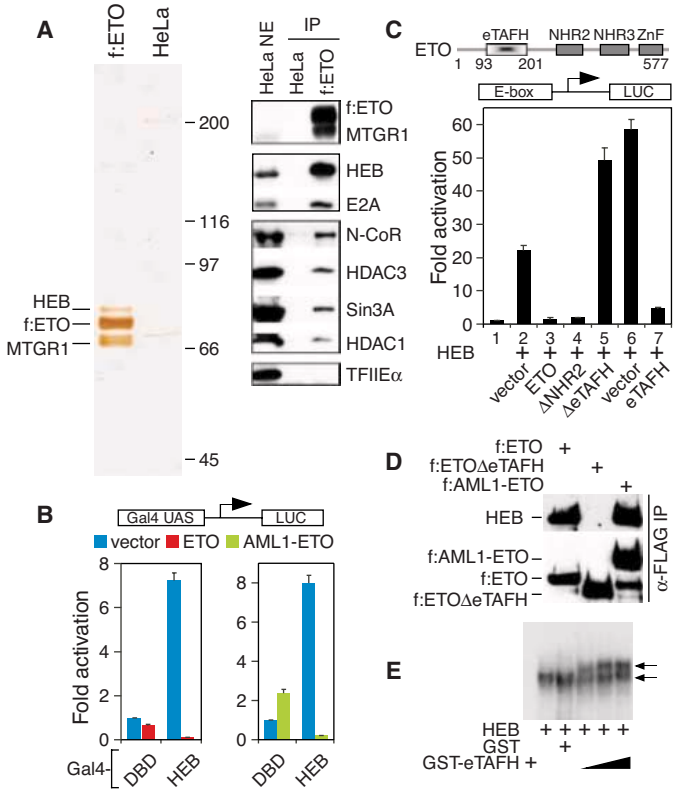

Fig. 1. ETO, through eTAFH, interacts with HEB and represses its transactivation function. (**A**) ETO interacts with HEB. (Left) Silver stain showing ETO-interacting polypeptides purified from FLAG-ETO–expressing cells. (Right) immunoblots of polypeptides purified as at left. (**B**) ETO and AML1-ETO inhibit HEB-dependent activation. (**C**) The eTAFH domain mediates inhibition of HEB-dependent activation. Luciferase assays in (B) and (C) used Gal4-based (B) or E-box–based (C) reporters and expression vectors as indicated at the bottom. (**D**) Requirement of eTAFH domain for ETO interactions with HEB in vivo, as revealed by immunoblot analysis of FLAG antibody immunoprecipitates (α-FLAG IP) from cells transfected with the indicated vectors (top). (**E**) eTAFH interacts with E-box–bound HEB, as revealed by electrophoretic mobility shift assay.

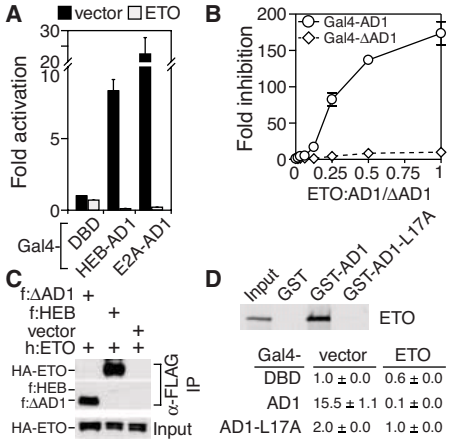

Fig. 2. ETO targets the E protein AD1 activation domain. (**A**) AD1 is sufficient for ETO-mediated inhibition. (**B**) AD1-independent HEB activity, unlike AD1 activity, is not inhibited by ETO. Luciferase assays in (A) and (B) were as in Fig. 1B, with the indicated vectors. (**C**) AD1 is required for HEB interaction with ETO in vivo (FLAG antibody coimmunoprecipitation/immunoblot assays were as in Fig. 1D). (**D**) An intact LXXLL motif is required for both physical [top, glutathione S-transferase (GST) pull-down assay] and functional (bottom, Gal4-based luciferase assay) interactions of AD1 with ETO as well as for maximal AD1-dependent activation. Note also the 155-fold (complete) inhibition of AD1 activity versus the twofold (incomplete) inhibition of the residual AD1-L17A activity.

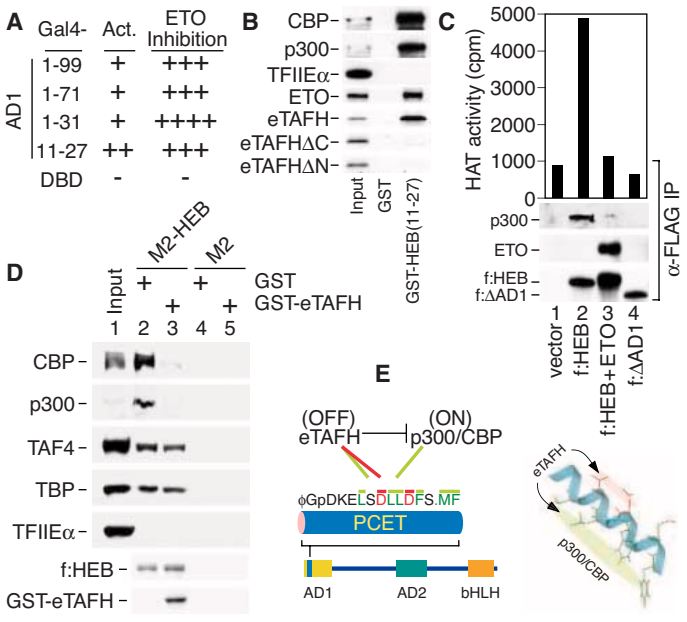

Fig. 3. ETO blocks p300/CBP recruitment by HEB. (**A**) The HEB(11-27) fragment is sufficient both for activation and for ETO-mediated inhibition. Ranges for fold activation and fold inhibition (assayed as in Fig. 2A) are as follows: +, 5 to 20; ++, 30 to 50; +++, 60 to 150; and ++++, >250. (**B**) PCET interacts with both p300/CBP and ETO or eTAFH. p300, CBP, and TFIIEα were from HeLa nuclear extracts; ETO and eTAFH and derivatives were translated in vitro. eTAFHΔC, residues 93 to 151; eTAFHΔN, residues 110 to 201. (**C**) ETO blocks AD1-dependent HEB interactions both with p300 and with HAT activity. FLAG antibody immunoprecipitates from cells transfected with indicated vectors (bottom) were analyzed by immunoblot (center) and for HAT activity (top). (**D**) Immunoblot analyses (top five panels) and Coomassie blue stain (bottom two panels) of polypeptides from HeLa extracts bound to M2-agarose–immobilized FLAG-HEB in the presence of GST or GST-eTAFH. (**E**) PCET functions as a control switch for E protein function. eTAFH recognizes distinct residues (red) in addition to residues (green) jointly recognized by eTAFH and p300/CBP. ϕ, Ile, Leu, or Val; p, Ser or Thr. The α-helical model of PCET at right shows distinct locations of at least two surfaces involved in eTAFH and p300/CBP interactions.

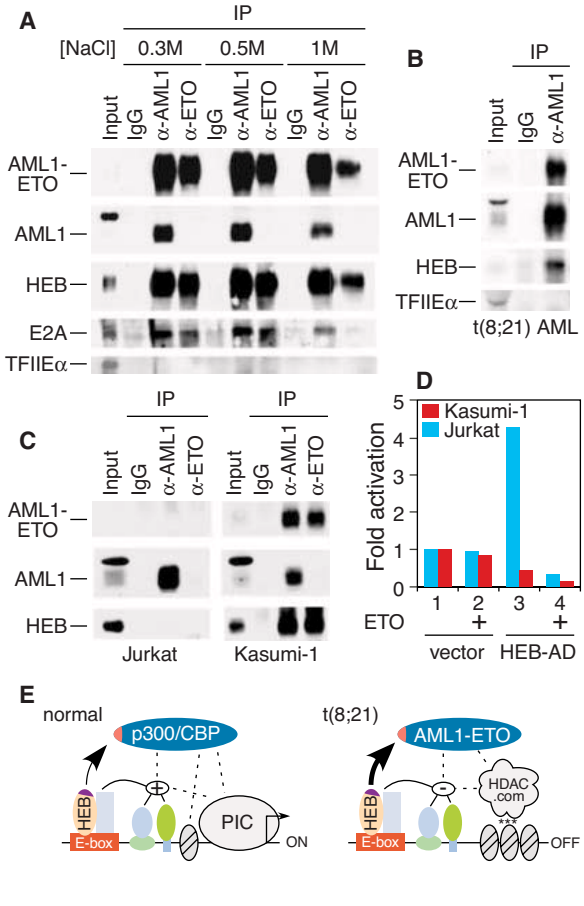

Fig. 4. AML1-ETO stably interacts with E proteins in t(8;21) leukemic cells. (**A** and **B**) Highly stable associations of endogenous E proteins with endogenous AML1-ETO in both Kasumi-1 (A) and primary t(8;21) leukemic (B) cells. (**C**) HEB interactions with ETO-containing polypeptide(s) are specific to t(8;21) cells. In (A) to (C), immunoprecipitates with indicated antibodies (top) were analyzed by immunoblot. (**D**) Suppression of ectopic HEB-dependent activity is specific to t(8;21) cells. Gal4-HEB AD was assayed in a Gal4-based Luciferase reporter assay in the presence and absence of ectopic ETO. (**E**) Model for AML1-ETO–driven aberrant cofactor exchange on E-box–bound E proteins such as HEB, and consequent E protein silencing in t(8;21) cells. Dashed lines indicate physical/functional interactions among cofactors or factors. eTAFH (and an equivalent region in p300/CBP) and PCET are shown in red and purple, respectively. Nucleosomes are shown as hatched gray circles. Promoter bound activators are shown as colored objects bound to DNA. HDAC.com, HDAC-containing complexes; pic, preinitiation complex.

described earlier, are important for recognition by both ETO and p300/CBP, adjacent Asp residues (red) provide additional separate surfaces specific for ETO (Fig. 3E, right). The differential recognition of these negatively charged residues may result in a greater affinity for ETO and consequently provides a structural basis for a dominant, and possibly irreversible, block of p300/CBP interactions by ETO.

We next explored the physiological relevance of these interactions to t(8;21) leukemogenesis by examining endogenous factors in t(8;21) leukemic cells. Kasumi-1 cells carry a t(8;21) translocation and express a high level of the AML1-ETO fusion protein but fail to express any detectable ETO protein (fig. S7A). Similar results were observed for another t(8;21) leukemic cell line (SKNO-1) (*7*). These data are consistent with earlier observations that ETO is not expressed in normal hematopoietic cells (*10*, *11*), and they further suggest that an ETO-associated activity could potentially contribute to t(8;21) leukemogenesis as a result of the aberrant high level of expression of AML1-ETO. In agreement with data presented above, endogenous HEB and E2A proteins were found in a very stable (resistant to 1% Triton X-100 and up to 1 M NaCl) natural complex(s) with AML1-ETO in Kasumi-1 cells (Fig. 4A). Similar analyses of SKNO-1 cells (fig. S7B) and of primary hematopoietic cells from a t(8;21) AML patient (Fig. 4B) further suggested that formation of a stable E protein:AML1-ETO complex is probably a general feature of t(8;21) cells. A control analysis failed to detect such interactions in a T lymphocyte cell line (Jurkat) (Fig. 4C) that does not express AML1-ETO (Fig. 4C) or detectable ETO (*7*). Thus, associations of E proteins, such as HEB, with an ETO-containing polypeptide in hematopoietic cells are probably dependent on the t(8;21) translocation and the consequent high level of expression of AML1-ETO.

As observed with ectopic ETO expression, a high level of expression of endogenous AML1-ETO in Kasumi-1 cells dominantly blocks p300 association with HEB and recruits HDACs to its AD1 domain (fig. S7, C and D, and supporting online text). These results clearly point to an AML1-ETO–dependent aberrant cofactor exchange for HEB, and likely other E proteins, in t(8;21) cells. Further supporting this idea, a Gal4-HEB activation domain (residues 1 to 548) fusion protein displayed an activation function in Jurkat cells, which do not express AML1-ETO, but not in Kasumi-1 cells, where a repression function is evident (Fig. 4D, lanes 1 and 3). This reflects an ETO-associated activity because ectopic ETO enhanced HEB silencing in Kasumi-1 cells and converted HEB into a repressor in Jurkat cells (Fig. 4D, lanes 3 and 4). Thus, an apparent consequence of the t(8;21) translocation is to allow a high level of expression of an ETO-containing polypeptide that is otherwise not expressed in normal hematopoietic cells (*10*,

11). Accordingly, in normal hematopoietic precursors (Fig. 4E, left), expression of essential (yet to be identified) genes for proper intracellular pathways [such as those involved in important checkpoint controls (*5*, *12*)] may be positively regulated by HEB (or other E proteins) through its promoter interactions with E-box elements (either as homodimers or as heterodimers with cognate partners), through its associations with p300/CBP HATs, and through the resulting cooperative interactions with adjacent promoter-bound activators. In contrast, in t(8;21) cells (Fig. 4E, right), expression of these genes may be silenced because of a dominant interaction of HEB with AML1-ETO that precludes promoter occupancy by p300/CBP but facilitates occupancy by HDAC-containing complexes. Inhibition of these gene expression events may thus predispose cells to further leukemogenic events, possibly as a result of dysregulated checkpoint control.

Beyond defining E proteins as AML1-ETO/ETO targets, our studies also elucidate an E protein silencing mechanism that is fundamentally different from that associated with Id proteins (inhibitors of DNA binding/differentiation) (*13*). Thus, although Id interactions with DNA binding regions of E proteins passively block corresponding promoter interactions, ETO/AML1-ETO interactions with AD1 of promoter-bound E proteins effect a silencing by directing an exchange of cofactors (HATs versus HDACs) that are recruited to target promoters. Like ETO, ETO-related proteins MTGR1 and ETO-2 similarly interact with and inhibit the function of E proteins (*7*). This mechanism may underlie a previously described context-dependent repressive function of the E protein AD1 domain and an enhancer-specific E protein activity (*14*).

E proteins (class A bHLH proteins) are ubiquitously expressed transcription factors that play key roles in the regulation of cell growth and differentiation and programmed cell death (*5*, *6*, *8*, *15*, *16*). E2A is essential for early B cell differentiation events and is a potential tumor suppressor (*6*, *15*). HEB has been implicated in both myogenesis and hematopoiesis (*5*, *17*). Fusions involving E2A (*5*) and HEB (*18*) AD1 domains are associated with leukemogenesis or tumorigenesis. Moreover, inhibition of E protein function by Id proteins negatively regulates cell differentiation and induces proliferation (*13*), an event whose dysregulation is often associated with oncogenesis. Similarly, and consistent with dysregulation of E protein functions by AML1-ETO, it has been shown that AML1-ETO directly induces aberrant hematopoietic cell proliferation (*19*), promotes extensive expansion and self-renewal of human hematopoietic stem cells (*20*–*22*) (the physiological target of many acute myeloid leukemias), and inhibits maturation of multiple lymphohematopoietic lineages (*23*), but is by itself insufficient for leukemogenesis (*24*). These observations further strengthen the idea that E proteins are major physiological targets of AML1-ETO in t(8;21) leukemogenic cells. Our results lead to the hypothesis that there are E protein target genes whose dysregulation by AML1-ETO may be important for t(8;21) leukemogenesis, and they set the stage for identification of these genes and for analyses of the structural basis of the underlying, newly defined regulatory factor interactions.

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25. Acknowledgements are presented in the supporting online material. Molecular interaction data have been deposited in the Biomolecular Interaction Network Database with accession codes 150973, 150974, 150975, 150976, 150977, 150978, 150979, 150980, 150981, 150982, 150983, 150984, 150985, 150986, 150987, 150988, 150989, 150990, 150991, 150992, and 150993.

Supporting Online Material

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Materials and Methods
SOM Text
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Small Interfering RNA–Induced Transcriptional Gene Silencing in Human Cells

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Small interfering RNA (siRNA) and microRNA silence genes at the transcriptional, posttranscriptional, and/or translational level. Using human tissue culture cells, we show that promoter-directed siRNA inhibits transcription of an integrated, proviral, elongation factor 1 alpha (EF1A) promoter–green fluorescent protein reporter gene and of endogenous EF1A. Silencing was associated with DNA methylation of the targeted sequence, and it required either active transport of siRNA into the nucleus or permeabilization of the nuclear envelope by lentiviral transduction. These results demonstrate that siRNA-directed transcriptional silencing is conserved in mammals, providing a means to inhibit mammalian gene function.

Small 21- to 25-nucleotide RNAs have diverse biological roles in eukaryotes, including transposon silencing and antiviral defense by small interfering RNAs (siRNAs) and developmental gene regulation by microRNAs (miRNAs) (*1*–*3*). siRNAs and miRNAs are processed from double-stranded precursors by the ribonuclease (RNase) III–RNA helicase Dicer (*1*). Argonaute proteins can bind small RNAs and are components of effector complexes that downregulate gene expression by several mechanisms (*4*). Small RNAs with perfect homology to their target can cause specific mRNA cleavage (called RNA interference), whereas those with mismatches to their target mediate translational inhibition (*3*). Small RNA–mediated transcriptional gene silencing was first observed in plants through the use of inverted-

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repeat transgenes or transgenic viruses to generate siRNAs homologous to a target promoter (*5*–*7*). Promoter-directed siRNAs also silence transcription in the yeast *Schizosaccharomyces pombe*, and transcriptional silencing in *Drosophila* has been linked to an Argonaute protein (*8*–*10*). Transcriptional silencing by siRNAs probably reflects genome defense mechanisms that target chromatin modifications to endogenous silent loci such as transposons and repeated sequences (*5*, *11*–*14*).

Although siRNA-induced transcriptional gene silencing has not been reported in mammals, transcription of an antisense RNA has been implicated in gene silencing and DNA methylation (*15*, *16*), and the structure of mouse pericentromeric heterochromatin may require an RNA component for its maintenance (*17*). Here we investigate whether siRNA-induced transcriptional gene silencing occurs in human cells.

We chose to target an elongation factor 1 alpha (EF1A) promoter–green fluorescent protein (GFP) reporter gene integrated into the genome of human 293FT cells by transduction with a feline immunodeficiency virus (FIV) vector (*18*). siRNA EF52 is homologous to an EF1A promoter sequence essential for transcription (AAG GTG GCG CGG GGT AAA CTG, –106 to –86 base pairs relative to the transcriptional start site) (*19*). A second siRNA homologous to exon 2 of the GFP coding region was designed to target posttranscriptional mRNA destruction. We transduced 293FT cells with the EF1A-GFP vector, allowed 24 hours for integration, then transfected with either EF52, GFP, or a control siRNA matching the human chemokine receptor CCR5. mRNA and DNA were analyzed 48 hours after siRNA transfection. The siRNA targeting the GFP mRNA transcript reduced expression relative to the control as measured by quantitative, real-time reverse transcription polymerase chain reaction (RT-PCR) (Fig. 1A). Potent inhibition of GFP expression was also seen with siRNA EF52 targeting the EF1A promoter (Fig. 1A, open bars).

Several lines of evidence indicate that inhibition of GFP expression by the promoter-directed EF52 siRNA occurs at the transcriptional level. Transcriptional silencing in mammalian cells is associated with chromatin modifications that include histone deacetylation and cytosine DNA methylation (*20*). Silencing by EF52 siRNA was reversed by treating cells with trichostatin (TSA) and 5-azacytidine (5-azaC), inhibitors of histone deacetylases and DNA methyltransferases, respectively (*20*) (Fig. 1A). These agents did not affect RNA interference of the GFP transcript. We confirmed transcriptional silencing using nuclear run-on analysis, which indicated a 93% reduction in transcriptional initiation from the EF1A-GFP reporter gene in EF52-treated cells (Fig. 1B). A glyceraldehyde-phosphate dehydrogenase (GAPDH) control was unaffected by EF52 siRNA in nuclear run-on and RT-PCR experiments. The GAPDH and CCR5 siRNA controls show that promoter-directed transcriptional silencing is specific (Fig. 1B and fig. S1B).

We performed several control experiments to exclude alternative explanations and to confirm that EF52 siRNA down-regulates EF1A-GFP expression by silencing transcription. To ensure that transcription from the integrated transgenic EF1A promoter initiated in a similar position to endogenous EF1A, we performed RT-PCR (fig. S2) (*19*, *21*). Specifically, transcripts containing the FIV rev-responsive element (RRE) upstream of the EF1A promoter were not detected, nor were other possible spliced messages initiating from the FIV long-terminal repeat (table S1 and fig. S2). These results show that siRNA EF52 targeted the transgenic EF1A promoter, not a transcribed region. Although the lentiviral vector used integrates into the chromosome and produces a transcriptionally active transgene within 24 hours (*22*), PCR analysis ensured that neither integration frequency nor total lentiviral DNA was affected by siRNA treatment (fig. S3). Collectively, these results demonstrate that EF52 siRNA targets a promoter region rather than transcribed RNA, does not reduce the number of transgenes, and induces transcriptional gene silencing in human cells.

Transcriptional gene silencing in mammalian cells is often accompanied by cytosine DNA methylation, and de novo DNA methylation in plants is guided by small RNAs (*12*, *20*, *23*). The EF52 siRNA target within the EF1A promoter contains a restriction site for the methylation-sensitive enzyme HinP1I. When methylated, this site is protected from digestion, and a PCR product spanning it can be amplified. The HinP1I site was unmethylated in genomic DNA from untreated cells and from cells treated with control CCR5 or GFP siRNAs. However, DNA methylation was detected in cells treated with EF52 promoter–directed siRNA (Fig. 2A) (the HinP1I

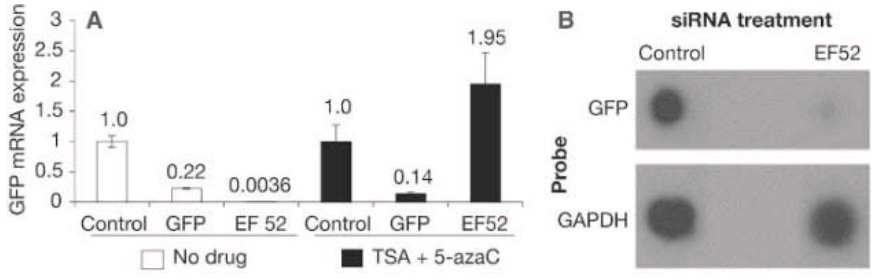

Fig. 1. (**A**) Promoter-targeted siRNA inhibits gene expression. 293FT cells were transduced in duplicate with lentivirus, then transfected with CCR5 (control), GFP (coding region), or EF52 (promoter) siRNAs. GFP mRNA was quantified by real-time RT-PCR. Gene expression was measured in triplicate; standard deviations are shown. (**B**) EF52 siRNA silences transcription. Nuclear run-on assays used nuclei from 293FT cells transduced with lentivirus and mock- or EF52 siRNA–transfected.

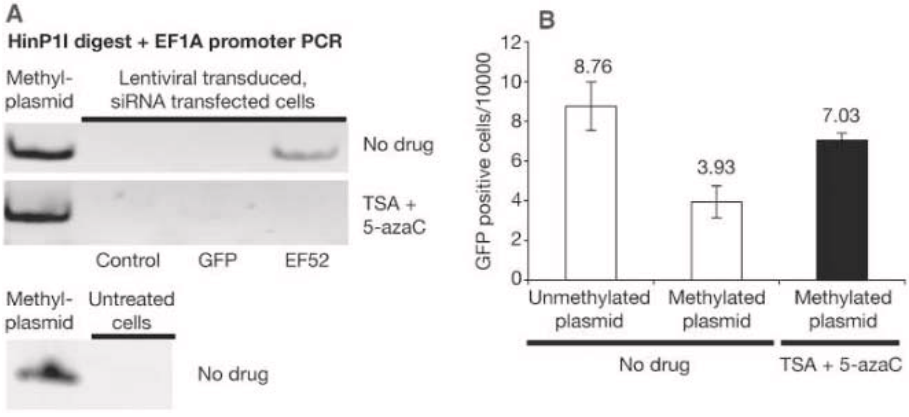

Fig. 2. siRNA-induced transcriptional silencing is associated with DNA methylation. (**A**) HinP1I-based DNA methylation assay of the EF1A promoter. DNA was prepared either (top) from lentiviral transduced cells transfected with CCR5 control, GFP, or EF52 siRNAs (with or without TSA and 5-azaC treatment) or (bottom) from untreated 293FT cells. HinP1I cut within the EF52 siRNA target site, preventing PCR amplification in unmethylated samples. Sss-I–methylated, EF1A-GFP plasmid DNA was a positive control. (**B**) Fluorescence-activated cell sorting analysis of GFP expression in cells transfected with Sss-I–methylated, EF1A-GFP plasmid, with or without TSA and 5-azaC treatment. TSA and 5-azaC counteracted transcriptional inhibition caused by DNA methylation. Standard errors of the mean are shown.

assay measured DNA methylation at both the endogenous locus and the EF1A-GFP reporter). Methylation induced by EF52 siRNA was abolished by treatment with TSA and 5-azaC (Fig. 2A). Gene expression from a transfected reporter plasmid was similarly reduced by exogenous methylation (with DNA methyltransferase Sss-I) and restored by TSA and 5-azaC (Fig. 2B). These findings show that siRNA-induced transcriptional silencing in mammalian cells is associated with DNA methylation, a mark of silent chromatin at other loci (*20*).

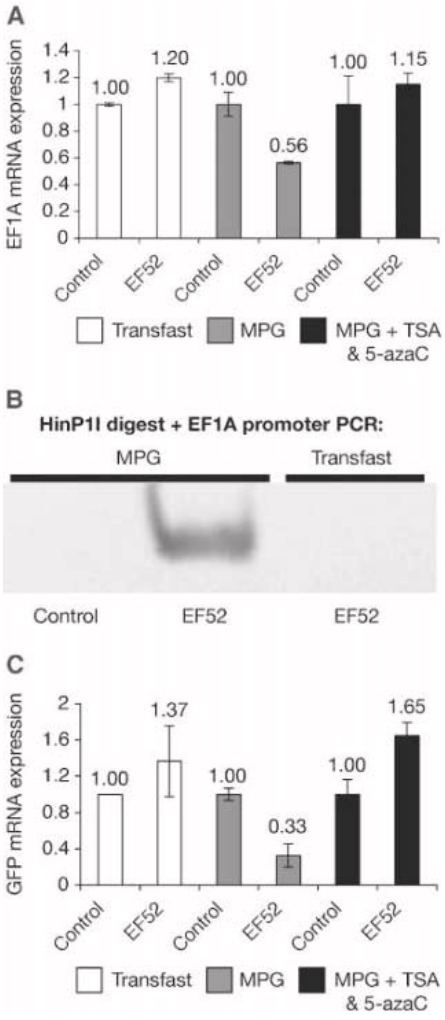

Fig. 3. (**A**) Promoter-targeted siRNA inhibits endogenous EF1A. EF1A expression was quantified by real-time RT-PCR in cells transfected with control (HIV-1 polymerase) or EF52 siRNAs with either MPG (a nuclear import–mediating peptide) or conventional Transfast reagent. Black columns represent MPG-transfected cells treated with TSA and 5-azaC. Standard errors of the mean were derived from four independent experiments. (**B**) siRNA-induced silencing of the endogenous EF1A promoter is associated with DNA methylation. DNA methylation of the endogenous EF1A promoter was assayed by the HinP1I method in cells that were transfected with control HIV-1 polymerase or EF52 siRNAs with either MPG or Transfast. (**C**) Nuclear-imported siRNAs inhibit transgenic EF1A-GFP long after lentiviral transduction. Lentiviral-transduced cells were sorted for GFP expression, grown for 8 weeks, then transfected as in (A). GFP mRNA expression was measured by real-time RT-PCR. The results represent two experiments with three independent samples per experiment; standard errors of the mean are shown.

It is clearly important whether endogenous EF1A expression is silenced by promoter-directed siRNAs. However, in mammalian cells that have not been transduced with lentivirus, transfected small RNAs lack an efficient nuclear transport mechanism, and mammalian cells have specialized export pathways for hairpin-containing miRNA precursors (*24*–*26*). This obstacle is circumvented by lentiviral transduction, which permeabilizes the nuclear membrane before siRNA transfection (*22*). In order to assess the effect of siRNA on the endogenous EF1A promoter, we transfected 293FT cells with EF52 and control [human immunodeficiency virus (HIV)–1 polymerase-specific] siRNAs using MPG, a bipartite amphipathic peptide incorporating a fusion peptide from HIV-1 gp41 transmembrane protein and the SV40 virus nuclear localization sequence (*26*). MPG facilitates the nuclear import of nucleic acids, including siRNAs (*26*). Cells transfected with EF52 and MPG showed significantly reduced endogenous EF1A expression by real-time RT-PCR, relative to the control (Fig. 3A). Transfection with EF52 and the conventional Transfast liposome reagent did not cause silencing, despite a transfection efficiency comparable to or greater than that of MPG (Fig. 3A). Silencing in cells transfected with EF52 and MPG was abolished by treatment with TSA and 5-azaC, indicating that it occurs at the transcriptional level (Fig. 3A). Furthermore, HinP1I digestion of the EF1A promoter was blocked in cells treated with EF52 and MPG, but not in cells transfected with EF52 and Transfast (Fig. 3B), indicating that siRNA-induced transcriptional silencing of the endogenous EF1A promoter is associated with DNA methylation.

As the effect of lentiviral transduction on the nuclear membrane is probably transient, we examined the need for nuclear transport of siRNAs in silencing an integrated EF1A-GFP reporter gene well after transduction (Fig. 3C). For this experiment, we transduced 293FT cells, isolated a GFP-positive population after 72 hours, and grew the cells for 8 weeks. As observed for endogenous EF1A, silencing of the integrated EF1A-GFP in this population depended on transfection with MPG and was reversed by TSA and 5-azaC (Fig. 3C). This suggests that siRNA-induced transcriptional silencing of an integrated reporter is not strictly dependent on lentiviral transduction, but rather on the ability of siRNAs to gain access to the nucleus. Silencing of endogenous EF1A and of the integrated reporter gene 8 weeks after transduction was less efficient than silencing of newly integrated EF1A-GFP (compare Fig. 3, A and C, to Fig. 1A). It is possible that MPG is less efficient than lentiviral transduction at transporting siRNAs into the nucleus. Alternatively, newly integrated EF1A-GFP transgenes may be more accessible to siRNAs because of their intrinsic chromatin structure; newly transformed transgenes are more susceptible to de novo DNA methylation and silencing in *Arabidopsis* (*26*).

Transfected siRNAs are generally retained in the cytoplasm of mammalian cells, where they mediate efficient mRNA cleavage but cannot target chromatin (*24*). siRNAs transcribed from hairpin transgenes are exported from the nucleus because they may resemble pre-miRNAs, which are produced by the nuclear RNase III Drosha and cleaved into mature miRNAs by cytoplasmic Dicer (*1*, *3*, *28*). These intrinsic features of mammalian cell biology may indicate why siRNA transport into the nucleus is necessary for transcriptional silencing.

Our findings confirm that siRNA-directed transcriptional gene silencing is conserved in mammalian cells. Small RNAs may guide mammalian transcriptional silencing in many different biological contexts, including the establishment of genomic imprints and targeting of DNA methylation to retroviruses and repeated transgenes (*12*, *29*, *30*).

Note added in proof: After this work was submitted, Fukugawa *et al*. showed that Dicer-defective chicken cells have heterochromatin defects at centromeres, possibly implicating siRNA in centromeric silencing (*31*).

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Impaired Degradation of Mutant α-Synuclein by Chaperone-Mediated Autophagy

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Aberrant α-synuclein degradation is implicated in Parkinson's disease pathogenesis because the protein accumulates in the Lewy inclusion bodies associated with the disease. Little is known, however, about the pathways by which wild-type α-synuclein is normally degraded. We found that wild-type α-synuclein was selectively translocated into lysosomes for degradation by the chaperone-mediated autophagy pathway. The pathogenic A53T and A30P α-synuclein mutants bound to the receptor for this pathway on the lysosomal membrane, but appeared to act as uptake blockers, inhibiting both their own degradation and that of other substrates. These findings may underlie the toxic gain-of-function by the mutants.

A30P and A53T mutations of α-synuclein, a cytosolic protein that normally exerts a presynaptic function (*1*), cause familial forms of Parkinson's disease (PD) (*2*). Because familial PD mutations in parkin and the ubiquitin carboxy-terminal hydrolase L1 (UCHL1) genes affect the ubiquitin-dependent proteasome proteolytic system, and mutations in the DJ-1 gene (*PARK7* gene on chromosome 1p36) are associated with the closely related sumoylation pathway, proteasomal degradation appears to be involved at least in some PD pathogenic pathways (*3*). Initial reports that α-synuclein is degraded through the proteasome (*4*, *5*) led to the idea that abnormalities in proteasomal degradation of α-synuclein underlie PD (*6*). Some subsequent studies failed to show alteration of α-synuclein levels by proteasomal inhibition (*7*–*9*), suggesting that there are alternate forms of α-synuclein degradation. Whereas proteins with short half-lives are mostly broken down by the proteasome, most cytosolic proteins with long half-lives (>10 hours) are degraded by autophagic pathways within lysosomes (*10*–*12*). Lysosomal inhibitors increase intracellular levels of α-synuclein (*13*–*15*), suggesting that α-synuclein may also be degraded by autophagy. Experimental overexpression of mutant α-synuclein activates macroautophagy, a form of autophagy in which large regions of cytosol are engulfed and trafficked to lysosomes (*12*). Although activation of macroautophagy degrades the mutant proteins (*13*, *16*) and mislocalizes synucleins to autophagic organelles (*17*), inhibition of macroautophagy does not appear to alter the degradation of wild-type α-synuclein (*15*).

In contrast to macroautophagy, a highly specific subset of cytosolic proteins with a motif recognized by the hsc70 chaperone are selectively degraded in lysosomes by a process known as chaperone-mediated autophagy (CMA) (*12*, *18*). Following binding of the chaperone-substrate complex to a lysosomal membrane receptor, lamp2a (*19*), CMA substrate proteins are translocated into the lumen for degradation by hydrolases (*18*, *20*).

We noted that the α-synuclein sequence contains a pentapeptide sequence ($_{95}$VKKDQ$_{99}$) that is consistent with a CMA recognition motif (*21*). In rat ventral midbrain cultures that contain dopaminergic neurons maintained in serum-free medium, we confirmed that the endogenous wild-type α-synuclein exhibited a relatively long half-life (16.8 ± 2 hours; Fig. 1A) (*22*). In contrast to the relatively small effect of epoxomicin, a selective proteasome inhibitor, on the half-life of α-synuclein (a 2.3-hours increase in half-life; Fig. 1A), ammonium chloride, which inhibits lysosomal proteolysis independently of the form of autophagy that delivers substrates to lysosomes, strongly inhibited α-synuclein degradation (9.6-hours increase in half-life; Fig. 1A). As described previously in PC12 cells for human wild-type α-synuclein (*13*), addition of 3-methyladenine, an inhibitor of macroautophagy, did not modify the degradation of rat α-synuclein (16.1± 2.4 hours). It thus appears that endogenous rat α-synuclein in ventral midbrain neuronal cultures is degraded in lysosomes but not by macroautophagy. We then examined the degradation of human wild-type α-synuclein expressed in PC12 cells (*16*), in which serum removal activates both macroautophagy and CMA (Fig. 1B). Serum removal markedly enhanced human α-synuclein proteolysis (from a half-life of 33.1 ± 6.3 hours to 19.7 ± 2.1 hours; n =5), whereas ammonium chloride inhibited its degradation (half-life of 48.9 ± 5.4 hours and 80.3 ± 16.6 hours, in the presence or absence of serum, respectively; n =5) (Fig. 1B) (supporting online text 1).

The presence of a CMA motif, however, does not guarantee that a protein is degraded by this pathway (*21*). The most direct test of whether a protein is a CMA substrate is to determine its binding, uptake, and degradation in isolated intact lysosomes (*19*, *20*, *23*, *24*). Because synuclein protofibrils have been suggested to destabilize the membranes of synthetic vesicles (*25*), we first confirmed that isolated lysosomes were not disrupted by wild-type or mutant α-synuclein proteins at concentrations as high as 70 μM (fig. S4B) (*22*). Under these conditions, we found that purified α-synuclein added to the incubation medium was translocated into and degraded by intact lysosomes, because lysosomal protease inhibitors increased

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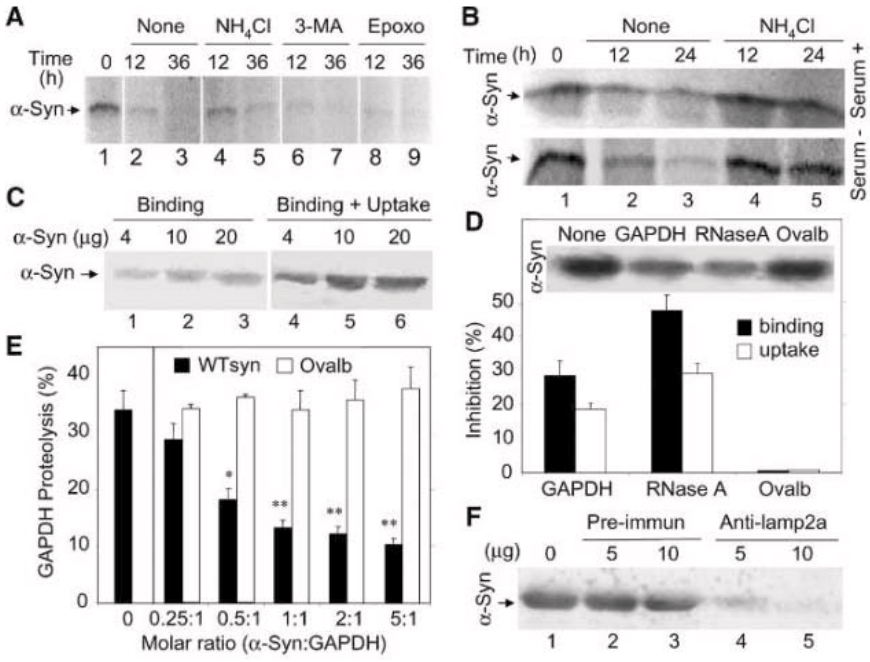

Fig. 1. Degradation of α-synuclein in lysosomes by CMA. (**A**) Effect of 15 mM NH_4Cl, 10 mM 3-methyl adenine (3-MA), or 10 nM epoxomicin (Epoxo) on the degradation of α-synuclein in ^{35}S-labeled rat ventral midbrain neuron cultures (*22*). The effects of these compounds on total rates of protein degradation in these cells are reported in the supplemental data (fig. S1A). (**B**) α-Synuclein immunoprecipitated from clonal PC12 cells stably expressing wild-type human α-synuclein (*16*) labeled as in (A) and maintained with (serum +) or without serum (serum −) and 15 mM NH_4Cl. Immunoprecipitation controls are shown in fig. S1B. (**C**) Association of increasing concentrations of α-synuclein with isolated lysosomes untreated (Binding) or previously treated with proteinase inhibitors (Binding + Uptake) (*19*, *20*, *23*, *24*). (**D**) Effect of a 2 M excess of glyceraldehyde-3-phosphate-dehydrogenase (GAPDH), ribonuclease A (RNase A), or ovalbumin (Ovalb) (*23*) in the lysosomal binding and uptake of α-synuclein analyzed by immunoblot as in (C). Percentages of inhibition are the mean + SE from four experiments. Inset shows a representative immunoblot for α-synuclein binding to lysosomes. (**E**) Effect of adding α-synuclein (WTsyn) or ovalbumin (Ovalb) at the indicated molar ratio with [^{14}C]GAPDH on the degradation of [^{14}C]GAPDH by intact lysosomes. Values are the mean + SE of four experiments (*$P < 0.05$; **$P <$ 0.01). (**F**) Effect of antibody blockade of the cytosolic tail of lamp2a on the binding of α-synuclein to isolated lysosomes.

levels of lysosomal-associated α-synuclein (Fig. 1C), and much of the α-synuclein associated to lysosomes was resistant to exogenously added proteases, demonstrating protection by the lysosomal membrane (fig. S4C) (*22*). The established CMA substrates glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and ribonuclease A (RNase A) (*20*, *23*) both inhibited lysosomal binding and uptake of α-synuclein into intact lysosomes, whereas ovalbumin, a protein which is not a CMA substrate, had no effect on α-synuclein binding or uptake (Fig. 1D). Consistent with a CMA substrate action, α-synuclein inhibited binding and uptake of GAPDH into isolated lysosomes (fig. S4D and Fig. 1F) but had no effect on GAPDH degradation by free lysosomal enzymes (see below); the differential inhibitory effects of different CMA substrates on binding and uptake may be related to differences in affinity for the binding and translocation components in the lysosomal membrane or to different unfolding requirements (*26*). As previously shown for other CMA substrates, blockade of the cytosolic tail of the lysosomal receptor using a selective antibody decreased the association of α-synuclein with lysosomes (Fig. 1F) (*19*). Finally, we mutated the sequence $_{95}$VKKDQ$_{99}$, consistent with a CMA recognition motif (*21*), by replacing DQ with AA, and found that, although the mutant ΔDQ and wild-type protein were similarly susceptible to degradation by lysosomal enzymes (fig. S4A), the association of the ΔDQ protein with the lysosomal membrane and its translocation into the lysosomal lumen was dramatically reduced (Fig. 2, A and B). Accordingly, GAPDH did not modify lysosomal binding of ΔDQ α-synuclein (Fig. 2A), and mutant

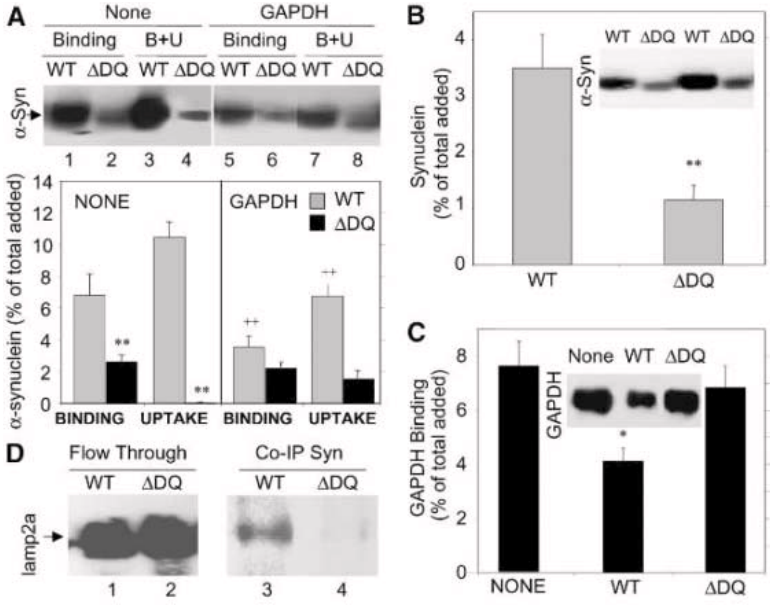

Fig. 2. A CMA targeting motif in α-synuclein. (**A**) Association of wild-type and mutant ΔDQ α-synuclein with isolated lysosomes untreated (Binding) or previously treated with proteinase inhibitors (binding + uptake; B+U). (Right) Effect of a 2 M excess of glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) on the association of wild-type and mutant α-synuclein to lysosomes (lanes 5 to 8). GAPDH inhibited 53.3 ± 3.2% and 42.8 ± 4.6% of wild-type α-synuclein binding and uptake, respectively, but did not have a significant effect on mutant α-synuclein binding or uptake. Values are the mean ± SE of six experiments. Uptake was calculated as in Fig. 1C. (**B**) Binding of wild-type and ΔDQ mutant α-synuclein to intact lysosomes at 0°C. Values are the mean ± SE from three different experiments. Inset shows a representative immunoblot with duplicate samples. (**C**) Binding of GAPDH to intact lysosomes alone (none) or in the presence of a 4 M excess of wild-type (WT) or mutant α-synuclein (ΔDQ). Values are the mean ± SE of three different experiments [(*) differences compared to WT; (+) differences comparing with and without GAPDH). (**D**) Immunoblot of lamp2a coimmunoprecipitated with wild-type and mutant α-synuclein incubated with intact lysosomes (*$P < 0.05$; **$P < 0.01$).

ΔDQ did not interfere with GAPDH binding (Fig. 2C). The mutant ΔDQ protein, in contrast to the wild type, did not bind the CMA receptor, lamp2a, at the lysosomal membrane (Fig. 2D). Thus, wild-type α-synuclein is internalized and degraded in lysosomes by CMA.

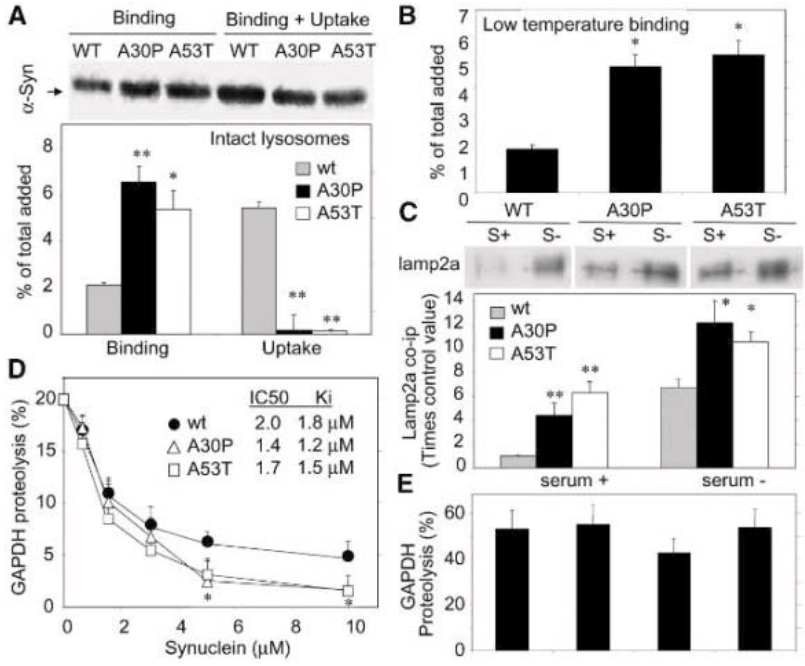

Fig. 3. Altered CMA of pathogenic α-synuclein mutants. (**A**) Binding and uptake of wild-type and A30P and A53T mutant α-synuclein by isolated lysosomes were measured as in Fig. 1C. Values are the mean ± SE of six different experiments. Inset shows a representative immunoblot. (**B**) Binding of wild-type and mutant α-synuclein to intact lysosomes at 0°C. Values are the mean ± SE from three different experiments. (**C**) Lamp2a coimmunoprecipitated with wild-type and mutant α-synucleins in the expressing PC12 cells maintained with (S+) or without (S−) serum. Values are the mean ± SE of three different experiments. Inset shows a representative immunoblot. (**D**) Effect of increasing concentrations of wild-type and mutant α-synucleins on the degradation of [^{14}C]GAPDH by isolated lysosomes. Values are the mean ± SE of three different experiments. Median inhibitory concentrations (IC_{50}) and inhibition constants (K_i) for each protein are shown. (**E**) Effect of a 5 M excess of wild-type or mutant α-synucleins on the degradation of [^{14}C]GAPDH by disrupted lysosomes. Values are the mean ± SE of two different experiments (*$P < 0.05$; **$P < 0.01$).

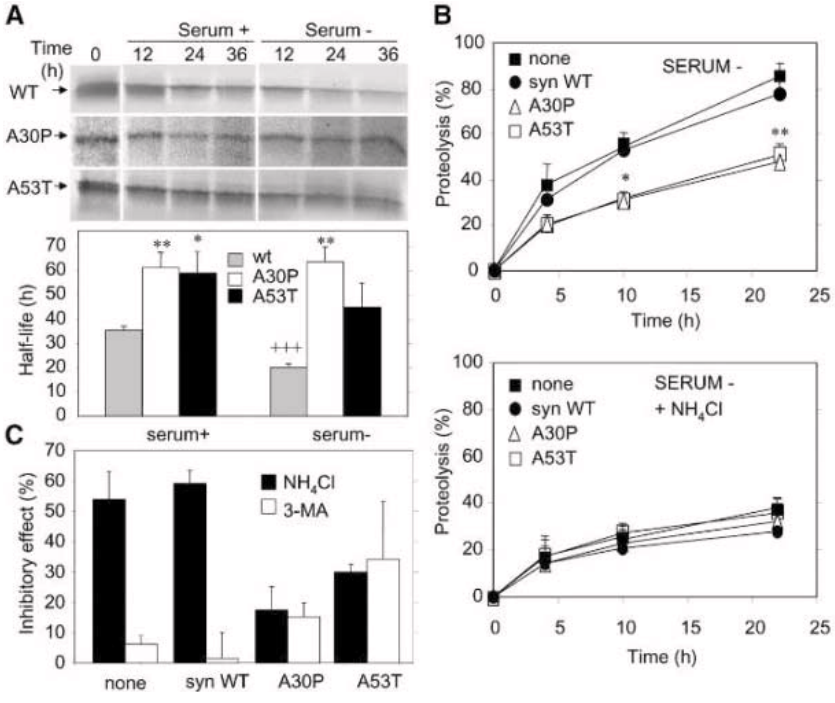

Fig. 4. Impaired CMA in cells expressing pathogenic α-synuclein mutants. (**A**) (Top) Degradation of wild-type (WT), A53T, and A30P human α-synuclein in stably transfected clonal PC12 cells was analyzed as in Fig. 1B. (Bottom) Half-lives of α-synucleins (from three experiments) calculated from measurements at 0, 12, 24, 36, and 48 hours [(*) differences compared to wild type; (+) differences comparing serum + to serum −; *$P < 0.05$, **$P < 0.01$, $^{+++}P < 0.001$]. (**B**) Degradation rates of long-lived proteins in serum-deprived PC12 cells (none) or PC12 cells stably expressing wild-type (WT), and mutant α-synucleins maintained without (top) or with 15 mM NH_4Cl (bottom). Values are the mean ± SE of three samples in two different experiments. (**C**) Inhibition of degradation of long-lived proteins in the cells described in (B) by 15 mM NH_4Cl or 10 mM 3-methyladenine (3-MA).

We then compared CMA of the pathogenic mutant and wild-type α-synuclein proteins in isolated lysosomes. Both A30P and A53T mutant α-synucleins bound intact lysosomes more strongly than did the wild-type protein, but the mutants were poorly internalized (Fig. 3A). The preferential binding of the mutant forms to this site was not simply a consequence of impaired uptake, because it was retained under lower temperature conditions in which the accumulation of substrates by CMA into the lysosomal lumen was blocked (Fig. 3B) (*23*). In cells expressing similar levels of wild-type and mutant α-synucleins, the amount of lamp2a that coimmunoprecipitated with mutant α-synucleins was higher than coimmunoprecipitated with the wild type (Fig. 3C; by twofold without serum and four- to sixfold with serum), confirming that the mutant proteins were tightly bound to the CMA receptor. As expected from their strong binding to the lysosomal receptor, the mutant α-synucleins inhibited GAPDH degradation in intact lysosomes more effectively than did the wild type (Fig. 3D). This inhibition was not due to an inhibition of proteolysis, because even a fivefold excess of all three forms of α-synuclein did not block degradation of GAPDH by free lysosomal proteases (Fig. 3E). Thus, the mutant forms of α-synuclein bound strongly to the CMA receptor on lysosomes but were not translocated into the lysosomal lumen, also impairing the degradation of other CMA substrate proteins.

Mutant α-synucleins were more stable than was the wild-type protein in PC12 cell clonal lines (Fig. 4A), and cells that expressed A53T or A30P mutant α-synuclein showed impaired autophagic degradation of proteins with a long half-life (Fig. 4B) (*22*). As in fibroblasts (*27*), once PC12 cells reached confluence, only a small fraction (5%) of total lysosomal protein degradation (sensitive to ammonium chloride) took place by macroautophagy (sensitive to 3-methyladenine) (Fig. 4C), and the same was true in PC12 cells that overexpressed wild-type α-synuclein. In contrast, PC12

clones overexpressing pathogenic α-synuclein mutants exhibited slower rates of long-lived protein degradation, and the remaining lysosomal protein degradation was completely blocked by 3-methyladenine, consistent with a blockade of CMA and compensatory activation of macroautophagy. These results could explain the degradation by macroautophagy of mutant, but not wild-type, α-synuclein proteins (*13*) (supporting online text 2). The induction of macroautophagy following blockade of normal CMA by mutant α-synucleins appears consistent with observations in cultured fibroblasts, in which blockade of CMA leads to compensatory activation of macroautophagy (*28*), as well as with the induction of neuronal macroautophagy by a number of stress paradigms, including the overexpression of the mutant α-synucleins (*16*, *29*).

Thus, wild-type α-synuclein is efficiently degraded in lysosomes by CMA, but the pathogenic α-synuclein mutations are poorly degraded by CMA despite a high affinity for the CMA receptor. Mutant α-synucleins blocked the lysosomal uptake and degradation of other CMA substrates. CMA blockade then results in a compensatory activation of macroautophagy which, under these conditions, cannot maintain normal rates of protein degradation. Impaired CMA of pathogenic α-synuclein may favor toxic gains-of-functions by contributing to its aggregation or additional modifications, such as nitrated or dopamine-adduct formation that could further underlie PD and other synucleinopathies (*3*). Mutant α-synuclein also inhibits the degradation of other long-lived cytosolic proteins by CMA, which may further contribute to cellular stress, perhaps causing the cell to rely on alternate degradation pathways or to aggregate damaged proteins.

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Supporting Online Material

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Distinct Ensemble Codes in Hippocampal Areas CA3 and CA1

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The hippocampus has differentiated into an extensively connected recurrent stage (CA3) followed by a feed-forward stage (CA1). We examined the function of this structural differentiation by determining how cell ensembles in rat CA3 and CA1 generate representations of rooms with common spatial elements. In CA3, distinct subsets of pyramidal cells were activated in each room, regardless of the similarity of the testing enclosure. In CA1, the activated populations overlapped, and the overlap increased in similar enclosures. After exposure to a novel room, ensemble activity developed slower in CA3 than CA1, suggesting that the representations emerged independently.

The hippocampus plays a fundamental role in encoding, consolidation, and retrieval of episodic and semantic memory (*1–4*). In mammals, the hippocampus has differentiated into a recurrent network of densely interconnected pyramidal cells (CA3) and a feed-forward network with almost no intrinsic excitatory connections (CA1) (*5*). These structural differences suggest distinct roles for CA3 and CA1 in hippocampal memory formation, but which functions are performed by the two subfields has remained elusive (*6*).

Firing properties of individual pyramidal cells in CA3 and CA1 offer limited clues about computational advantages of hippocampal differentiation. In both subfields, the majority of pyramidal cells have place-specific firing fields controlled by geometric relations in the animal's local environment (*2*, *7–10*), and there are only small quantitative differences in their spatial firing characteristics (*10*). However, cell assemblies in CA3 and CA1 may contain additional information (*11*). A major function of such assemblies may be to augment differences between correlated input patterns (*1*, *8*, *12–18*) so as to minimize interference between stored information (*19*). To examine whether such an orthogonalization process (pattern separation) (*20*) is implemented differentially in CA3 and CA1, we compared ensemble firing in connected segments of these areas (*5*) (Fig. 1A) while rats were chasing food in enclosures with varying geometric similarity (large square, small square, and small circle) in three different rooms (A, B, and C).

Individual place cells in CA3 and CA1 had similar firing characteristics (*7*, *10*, *21*) (Fig. 2A and tables S1 and S2). The most obvious difference was the significantly lower proportion of active neurons in CA3 (*10*). With a rate threshold of 0.25 Hz, the

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proportion of active cells ranged from 0.17 (B) to 0.32 (A) in CA3 and from 0.48 (C) to 0.66 (A) in CA1 (z values from 4.1 in C to 8.0 in A, $P < 0.001$) (Fig. 1, B to D, and fig. S1). The sparser firing of CA3 may indeed favor more orthogonal representations, but it cannot be established from discharge profiles in a single condition whether active orthogonalization takes place. To examine orthogonalization processes more directly, we quantified the extent to which the active set of neurons overlapped between two familiar rooms (A and B) by using a measure that takes into account the passive effect of different sparsity in CA3 and CA1 (Fig. 2B).

The analyses indicated that ensemble codes in CA3 and CA1 are different (Fig. 2B). In CA3, representations for A and B were nearly independent. The measured overlap ranged from 0.11 to 0.14 for the four possible comparisons of A and B (AB, AB′, A′B, and A′B′, where A and B are the first 10-min blocks in each room and A′ and B′ the second). These values were not significantly different from the expected overlap for independent firing, which ranged from 0.12 to 0.14 depending on exact firing rate distributions between A, B, B′, and A′ (Fig. 2B) (t values between 0.1 and 1.2). The distribution of CA3 population vectors was highly informative about which room the rat was in [0.54 ± 0.06 bits at time bin (τ) = 150 ms, mean ± SEM]. In CA1, however, there was significant overlap between the representations for A and B. Observed values ranged from 0.36 to 0.42, whereas expected values were between 0.26 and 0.28 (t values between 3.7 and 5.2, all $P < 0.001$). Population vectors differed less than in CA3 [0.30 ± 0.05 bits for CA1 at τ = 150; $t(17) = 3.2$, $P < 0.005$].

We hypothesized that the correlated activity in CA1 depended on the distinctness of A and B and thus compared the overlap obtained with similar and different enclosures in these rooms (Fig. 2C and figs. S2 and S3). Shared features had no effect in CA3 (Fig. 2C). With identical square boxes in A and B (high similarity), the overlap in CA1 was almost as large as with repeated testing in the same room (0.55 for AB versus 0.63 for AA′ and 0.66 for BB′). With squares of different size (medium similarity), the overlap decreased to 0.43. With boxes that differed both in size and shape (low similarity), the overlap was no longer distinguishable from the expected value obtained with random permutations (0.32 versus 0.28). These effects were statistically significant [$F(2,140) = 6.0$, $P < 0.005$] and consistent across animals (high similarity values were 0.56 and 0.54; medium similarity, 0.53, 0.45, and 0.32; low similarity, 0.41, 0.34, and 0.27). These effects were also seen in spatial correlations between pairs of firing fields in A and B (Fig. 2D) and in the temporal structure of the ensemble activity (Fig. 2E) [Supporting Online Material (SOM) Text].

Place fields develop as animals explore novel environments (*2*, *9*). We asked whether differences between CA3 and CA1 emerge gradually or are present from the beginning in rats exposed to a novel room (room C) (Fig. 3). In CA3, the overlap between C and A or B fluctuated around expected values (0.16 versus 0.14) [$t(83) = 0.79$, NS], implying that new representations were decorrelated already on the first trial (Fig. 3B). In CA1, the new representations correlated significantly with those in A and B [overlap of 0.38; expected value of 0.24; $t(104) = 4.6$, $P < 0.001$]. This overlap in CA1 was not influenced by the geometry of the enclosures (Fig. 3B) [$t(63) = 0.0$ for medium versus low similarity].

To determine whether the ensemble codes in CA1 derive from those in CA3, we next compared their time courses. In CA3, the new spatial map stabilized only after 20 to 30 min in C (Fig. 3A). The overlap between the first and the last 10-min blocks (CC′′) was low compared to the overlap between repeated trials in the familiar rooms (AA′ and BB′) (Fig. 3C versus Fig. 2B). The distribution of population vectors was more different between the first and the last 10 min (CC′′) than between the first and the middle 10 min (CC′) (Fig. 3, D and E) (SOM Text), suggesting that the stabilization of the ensemble structure in CA3 took 20 min or more. In simultaneously recorded CA1 cells, reliable place fields were mostly apparent already during the first minutes (*9*). The overlap between the first and last 10 min was higher than that for CA3 [$t(91) = 5.1$, $P < 0.001$] (Fig. 3C), and the population-vector distributions were more similar (Fig. 3, D and E) and not significantly different from those obtained between repeated tests in A or B (SOM Text). The faster manifestation of an ensemble code in CA1 suggests that representations in CA3 and CA1 arise independently and that the latter may emerge through direct input from the entorhinal cortex (*22*).

The functional differences between CA3 and CA1 suggest a rationale for the differentiation of their intrinsic structure (*6*).

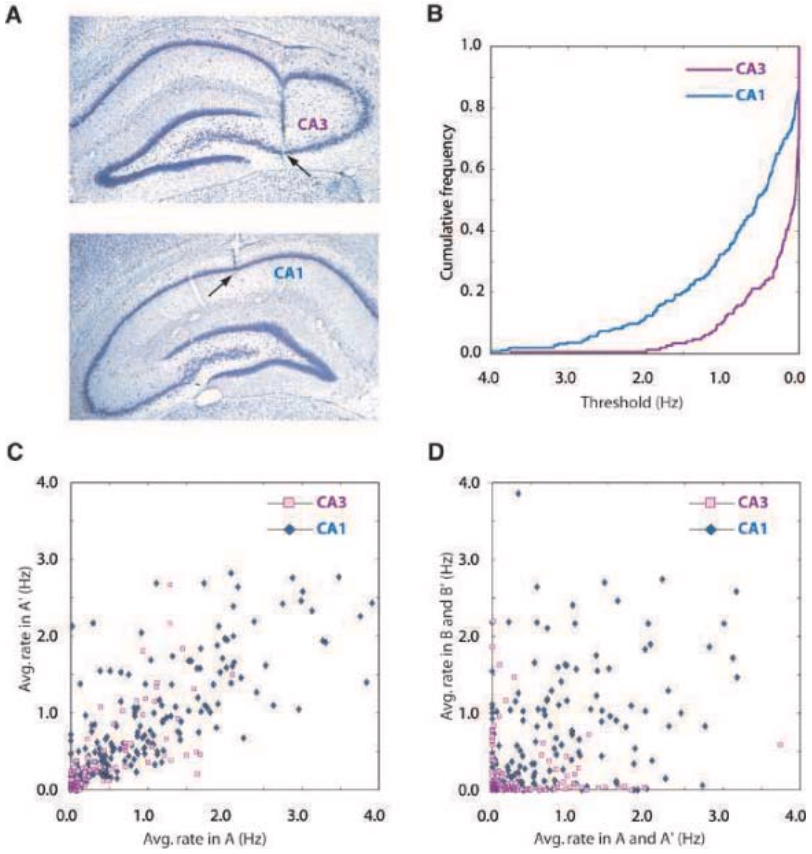

Fig. 1. Sparser representations in CA3 than CA1. (**A**) Representative electrode locations (arrows) in CA3 and CA1 (same rat). (**B**) Cumulative frequency diagram showing lower proportion of active cells in CA3 than CA1 in room A (all cells; see also fig. S1). (C and D) Relation between firing rates on repeated tests in the same room (**C**) or in different rooms (**D**). Each point corresponds to one cell.

With its orthogonalized activity patterns, CA3 may store accurate representations of context one in one, with the representation of local position by individual neurons. This provides a neuronal substrate for the observation that animals with hippocampal lesions show increased susceptibility to interference (*19*) and fail to discriminate between contexts with different conditioning histories, particularly when the contexts differ only minimally (*23*, *24*). As input similarity increases, the CA3 network may eventually switch from pattern separation to pattern completion (*1*, *12*, *25*, *26*), resulting in a larger overlap in CA3 than in CA1 (*26*) and suggesting that CA3 contains coherent but flexible population codes that can be used both to disambiguate and to identify contexts (*27*). Taken together, the findings imply that encoding of context, defined as the relations between stimuli and the time and place in which events occur, may be a major function of CA3 (*2–4*, *28*, *29*). Although pattern separation and pattern completion probably arise within the dentate/CA3 complex (*13*, *15*), the exact contribution of the dentate to ensemble activity in CA3 remains to be elucidated.

In contrast to CA3, population codes in CA1 responded to common features of the rooms. When rats were tested with identical boxes in two different rooms, representations in CA1 were only weakly more different than during repeated recording in the same room. This suggests that place cells in CA1 can respond to individual landmark configurations independently of background context, as observed after cue misalignments in CA1 (*26*, *30*, *31*) (SOM Text). However, orthogonalized codes from CA3 may be reflected in equally orthogonal representations in CA1 under certain conditions, such as with low sensory input and during memory-based behavior. The orthogonalized codes may then be exported to other brain structures (*32*, *33*), associating a contextual tag to information stored there.

New representations formed at a slower rate in CA3 than in CA1. The slower manifestation of a stable map in CA3 may, perhaps, reflect the predominantly recurrent nature of interactions in this network, which may require that a stable orthogonalized representation of a new context be reached iteratively. In contrast, the population activity in the predominantly feedforward network of CA1 may be established at the very beginning of the trial or even be available beforehand, hardwired in the circuit (*27*). The faster appearance of the CA1 ensemble code suggests that it emerges independently of the CA3 representation, probably via the direct projections from entorhinal cortex (*22*). However, representations in CA1 may still evolve further. The relation between geometric similarity and overlap was not expressed on day 1 in the novel room, suggesting that the more limited disambiguation of differences in CA1 is a later refinement, like other

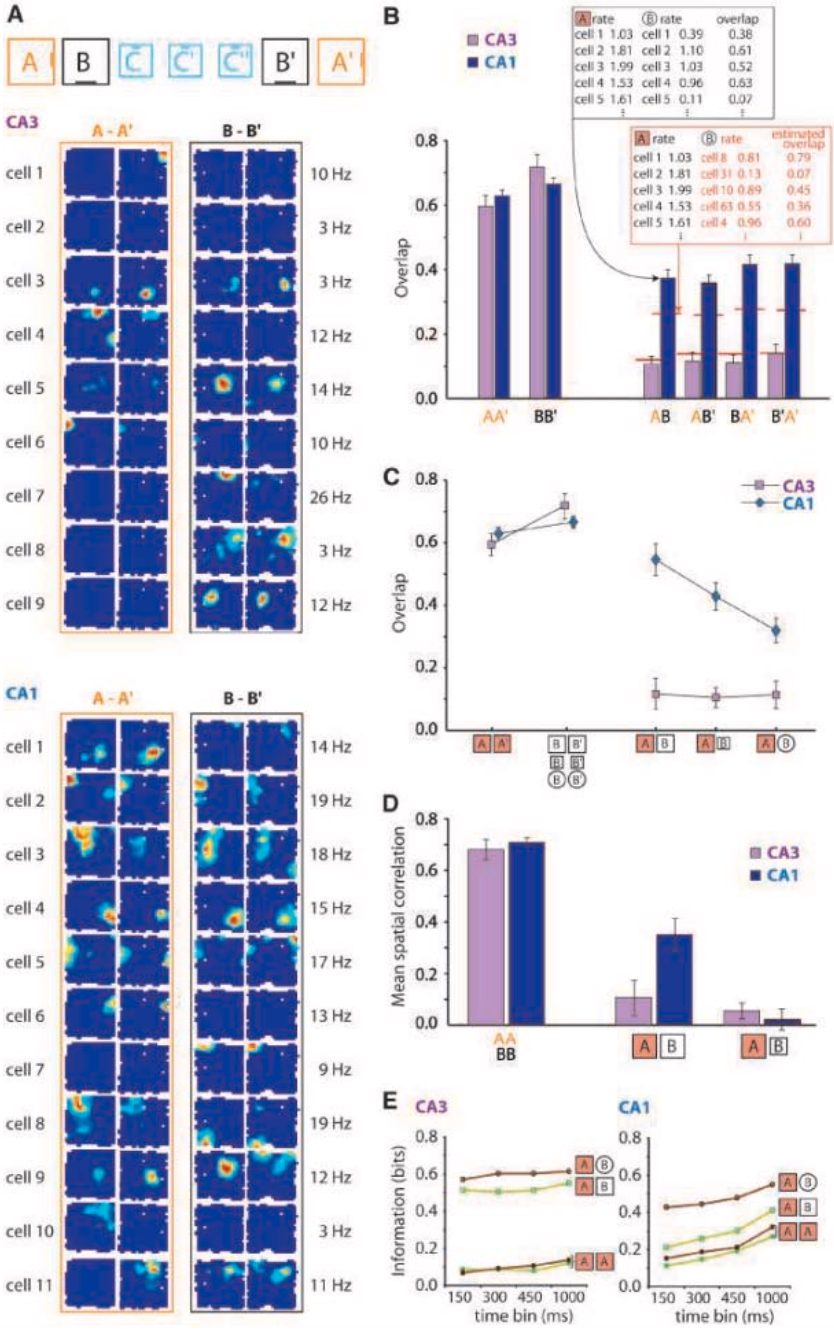

Fig. 2. Orthogonalized representations in CA3 but not CA1. (**A**) Color-coded rate maps showing place fields in identical enclosures but different rooms (day 10). Top section indicates recording sequence, geometry of test enclosures, and orientation of cue card (lines inside boxes). Spikes were recorded simultaneously from CA3 and CA1. Rows show cells; columns show trials in rooms A and B (not chronologically ordered). Plots are scaled to indicate maximum rates (red, maximum; blue, silent; white, not visited). (**B**) Overlap between active populations in rooms A and B (mean ± SEM). Overlap was measured by averaging across cells the ratio between the lower and higher rates in a pair of trials (top inset). Red lines indicate overlaps expected by assuming independent firing in the two trials (bottom inset). (**C**) Overlap as a function of geometric similarity of the enclosures in rooms A and B. (**D**) Mean spatial correlation (± SEM) of place fields in rooms A and B (squares only) (SOM Text). (**E**) Effect of geometric similarity on ensemble coactivity in CA1 but not CA3 in two rats with more than eight simultaneously recorded cells in each area (brown, low similarity session; green, high similarity session). High information corresponds to distinct distributions of population vectors in rooms A and B.

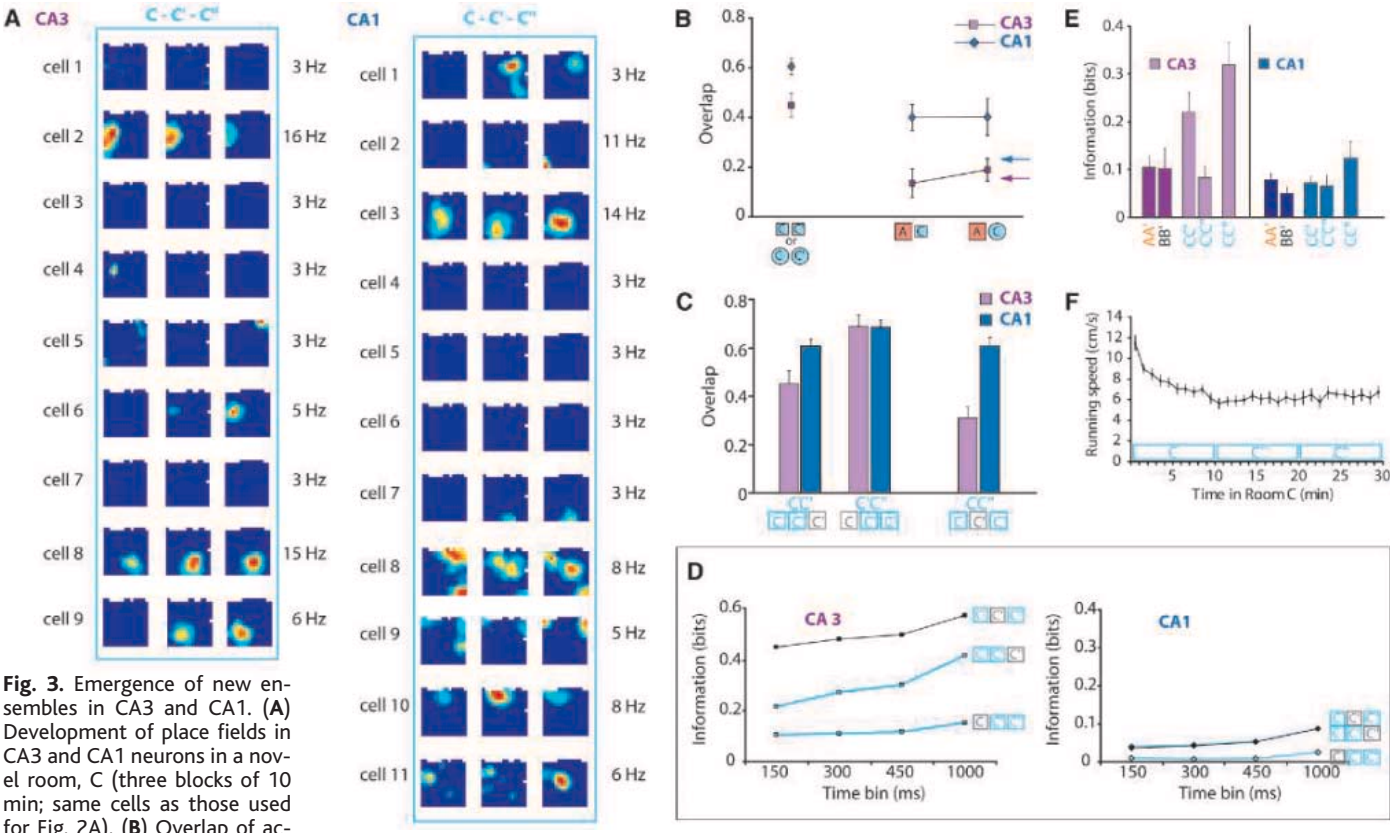

Fig. 3. Emergence of new ensembles in CA3 and CA1. (**A**) Development of place fields in CA3 and CA1 neurons in a novel room, C (three blocks of 10 min; same cells as those used for Fig. 2A). (**B**) Overlap of activity between rooms A (familiar) and C (novel). Enclosures had different sizes or both different sizes and different shapes. Arrows indicate expected values (purple, CA3; blue, CA1). (**C**) Overlap between pairs of 10-min blocks in room C (C, 0 to 10 min; C′, 10 to 20 min; C′′, 20 to 30 min). (D and E) Development of ensemble structure in CA3 and CA1 [(**D**) same experiment as in (A); (**E**) whole sample]. The difference in neuronal activity between early and late blocks of the trial was assessed by measuring how much information the distribution of population vectors provided about the part of the trial that was being recorded. (**F**) Horizontal speed during exploration of room C (mean ± SEM).

delayed changes of ensemble activity in this subfield (*34*, *35*). Whether these slower processes reflect the integration of inputs from CA3, conveying orthogonalized memory representations, with processed sensory information carried to CA1 by direct inputs from entorhinal cortex, remains to be determined.

Note added in proof: Additional evidence for CA1-CA3 differences is provided by a recent study measuring immediate early gene activation in two different novel rooms (*36*).

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20. Orthogonalization (pattern separation) refers to the tendency to decorrelate representations, assessed relative to the baseline expected for unrelated conditions. Orthogonalization is expressed as a difference in both the subset of active cells and the relative firing locations of cells that were active in each of the conditions (SOM Text). Remapping is a special case limited to the spatial domain.
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Supporting Online Material

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Materials and Methods
SOM Text
Figs. S1 to S3
Tables S1 and S2
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FACULTY POSITIONS 2: Judging Joint Appointments

AS LIFE SCIENCE TURNS EVER MORE INTEGRATED, INCREASING NUMBERS OF ACADEMICS MAY BE OFFERED OR MAY DESIRE JOINT APPOINTMENTS IN THE FUTURE. DEPENDING ON THE STAGE OF A SCIENTIST'S CAREER, A JOINT APPOINTMENT CAN BE A BOOSTER ROCKET OR AN ANCHOR. THE QUARTET OF EXPERTS INTERVIEWED HERE HELP YOUNG SCIENTISTS MAKE THE BEST OF JOINT OPPORTUNITIES. BY MIKE MAY

With phrases like systems biology and transitional science taking the forefront of today's life sciences, many researchers scramble for more breadth. For some scientists, that breadth comes—in part—from developing joint appointments. Brian H. Davison, director of the life sciences division at Oak Ridge National Laboratory, knows the ups and downs of multiple responsibilities. He has served as leader of the biochemical engineering research group, director of the Bioprocessing Research and Development Center, as chair of the institutional biosafety committee, and as an adjunct at the University of Tennessee. In thinking of a joint appointment, he says, "It offers broad access to a range of scientists, capabilities, and equipment." He adds, "You can potentially double your number of collaborators that are institutionally available."

In addition to more colleagues, a joint appointment can also bring a faculty member more students. "You get access to graduate student pools," says Harris Lewin, professor of immunogenetics and director of The Institute for Genomic Biology at the University of Illinois at Urbana-Champaign. He adds, "It also gives you more ways to target grants." Because of added access to students and equipment, plus an edge on grants, Lewin says, "Senior faculty should get as many joint appointments as possible."

Still, joint appointments generate challenges, too. David Sabatini, associate member of the Whitehead Institute for Biomedical Research and assistant professor of biology at the Massachusetts Institute of Technology, says, "You face more obligations because you are under more umbrellas." Brian G. Van Ness, head of the department of genetics, cell biology, and development and jointly appointed to the department of biochemistry at the University of Minnesota, adds, "A joint appointment means that I have too many meetings to go to." Despite the extra work and added responsibility, Van Ness adds, "The obvious advantage is that we benefit from the synergy of expertise."

- **Massachusetts Institute of Technology** (http://web.mit.edu/)
- **Oak Ridge National Laboratory** (http://www.ornl.gov/)
- **University of Illinois at Urbana-Champaign** (http://www.uiuc.edu/)
- **University of Minnesota** (http://www1.umn.edu/twincities/index.php)

Creating Your Own Box

In today's business world, people often hear the phrase, "Think outside the box." To get the best faculty jobs, though, a young scientist needs to go a step beyond the usual boxes. Instead, the top young scientists create their own boxes—research areas that are largely unique. When asked what kind of scientists are most marketable for faculty positions, Davison replies, "people who don't sit in any conventional box." He adds that those people need a strong knowledge of biology in general, but also must gain expertise in another area, such as chemistry, physical science, or computation. Other experts also encourage a variety of skills. Van Ness, says, "We are looking for people who take integrated approaches to developmental biology and also have clinical expertise or a knowledge of general biology, chemistry, or biochemistry." CONTINUED »

FACULTY POSITIONS 2

BRIAN H. DAVISON

Some of the most employable areas, though, remain the popular ones of the past few years. Lewin says that the most desired skills are "genomics coupled with anything." By genomics, he means any of the 'omics fields. He likes to see people who understand comparative and functional genomics and have a background in electrical engineering, robotics, or computer architecture. He adds, "It is very useful right now to have experience with a nontraditional model system that has a sequenced genome or that is on the list to be sequenced soon." He points to dog and pig as biomedical models of metabolic disorders or transplantation, respectively. The list of interesting animals, according to Lewin, also includes sea urchins and sea squirts—essentially any animal with a known, or soon to be known, genome sequence.

Sabatini agrees that potential faculty members get the most attention if they are skilled in some nontraditional animal system. "We understand lots about model organisms," he says. "Let's move higher up to mammalian systems in general." In that move, life science research will evolve further from a focus on individual proteins and molecules to whole systems. "Physiology represents the ultimate in systems biology," Sabatini says. "Now, it seems to me that the emphasis is on big questions—through the organ and organismal level and using an integrative approach." On the other hand, Sabatini cautions that life science makes up a big area, and it is very hard to know what will be hot even one day ahead.

Minding the Masters

Although a joint appointment puts a faculty member in touch with more colleagues and students and provides access to more equipment, it also makes for more bosses. "A joint faculty member serves multiple masters," says Davison. "If there are problems, it is usually where the expectations of the two masters are not clear, and a scientist comes in and does not know what must be done to keep each side happy." He adds, "Sometimes you can please one and not the other." In the end, failure to please them both can dissolve a joint appointment.

Lewin agrees that a joint appointment can create more hurdles. He says, "You may have two departments or two colleges voting on your tenure, and they may have different requirements." A young faculty member might meet one set of requirements and not the other. "It's hard enough to get through one department," Lewin adds.

Consequently, a joint appointment may not suit new faculty members. But for those who want to go joint anyway, it pays to make sure that the rules are clear from the very beginning. A potential joint faculty member should make sure—and get in writing—the expectations of both departments or institutions that would be involved. In addition, it must be made clear if the faculty member must pass the tenure requirements of both groups, or if some compromise solution will suffice. Lewin emphasizes, "You need to know the requirements for each unit involved."

BRIAN G. VAN NESS

Sizing Up Your Spot

No matter where a young faculty member hopes to land a job—single or joint appointment—the experts interviewed here pass along some general advice. "The first thing you need is access to other people with great minds," says Lewin. "So pick a place with proximity to great scientists."

Modern life science research, though, needs machines as well as minds. "You need access to shared core facilities," adds Lewin. "You won't be able to do biology with a microscope and a centrifuge. You need microarray facilities, DNA sequencers, and tools for proteomics, metabolomics."

In addition, Lewin and Sabatini both mentioned the need for a good pool of potential students. "The quality of students at the beginning really matters," says Sabatini, "because when you start a lab you can get high quality students sooner than postdocs. So make sure that there are good students to be had." Moreover, a good job provides a large student pool to select from. On the other hand, a new faculty member should not have too much contact with students when it comes to teaching. Lewin says, "Look for a fair teaching load—maybe a graduated load that starts with no teaching and then increases to one course a semester or one course a year after the second year."

At the start, the free time from teaching lets a new faculty member start a lab. Even for those without joint appointments, that lab work can involve collaboration. Van Ness says, "In my day, you came in to develop expertise on your own. Now, new faculty members often walk in the door interested in collaborative arrangements and cooperative opportunities." As life scientists participate increasingly in systems biology and transitional science, the faculty members of the future might depend on cooperation on many levels.

Mike May (mikemay@mindspring.com) is a freelance writer and editor based in Madison, Indiana, U.S.A.

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

CAMPUS-WIDE FACULTY HIRING INITIATIVE IN BIOINFORMATICS

The University of Illinois at Urbana-Champaign is rapidly scaling up faculty hiring in bioinformatics to meet the needs of its research, education, and outreach programs. New faculty will be expected to contribute to major campus thrusts in Systems Biology, Cellular and Metabolic Engineering, and Genome Technology. Faculty hiring will be based in one or more highly ranked academic departments, with a joint appointment possible in the Institute for Genomic Biology (IGB), the National Center for Supercomputing Applications (NCSA) and the Center for Nanoscale Science and Technology (CNST).

Department of Bioengineering

The Department of Bioengineering, the newest department in the nationally top-ranked College of Engineering at UIUC, invites applications for several full-time, tenure-track or tenured professor positions in bioinformatics and computational biology. These faculty will design a new computational bioengineering curriculum and help build the bioinformatics research program at the new flagship interdisciplinary research facility on the UIUC campus, the Institute for Genomic Biology. Further application information, including other faculty openings, closing application date, and starting employment dates, is detailed on our website www.bioen.uiuc.edu. For further information call (217)333.1867 or email bioen@uiuc.edu. *UIUC is an AA-EOE.*

Department of Chemical and Biomolecular Engineering

The Department of Chemical and Biomolecular Engineering invites applications for full-time, tenure-track faculty positions to begin August 16, 2005, in the area of bioinformatics, defined to encompass all aspects of collecting, analyzing, and using biological data at the interfaces among biological, chemical, computer, engineering, and medical sciences. Closing date is January 1, 2005. Applications with curriculum vitae, research and instruction statement, and names of three references should be sent to Professor Deborah Leckband, Head of Chemical and Biomolecular Engineering, 114 Roger Adams Lab, Box C-3, 600 S. Mathews Ave., Urbana, IL 61801 (phone: (217)333.3640; email: kljohns@uiuc.edu). For more information see www.chemeng.uiuc.edu. *UIUC is an AA-EOE.*

Department of Computer Science

The Department of Computer Science invites applications for one or more full-time, tenure-track and tenured professor positions to begin August 16, 2005, in bioinformatics and computational biology. Candidates are expected to contribute to our new Masters degree program in Bioinformatics and will have the opportunity to become involved with research at the Institute for Genomic Biology. Applications should be received on or before December 1, 2004. Please submit your curriculum vitae, statements of research and teaching, and names of three references online at: www.cs/employment/faculty.html. For more information please send email to admin@cs.uiuc.edu. *UIUC is an AA-EOE.*

Department of Microbiology

The Department of Microbiology solicits applications for a full-time, tenure-track assistant professor in bioinformatics and computational biology beginning August 2005. The individual sought for this position should be able to develop novel data-mining and pattern recognition tools to identify new biosynthetic pathways from sequenced microbial genomes, develop new algorithms for reconstructing metabolic and biosynthetic pathways, and build computational models for metabolic networks and for generating global physiomic profiles by integrating data from genomics, proteomics, and metabolomics studies. Candidates with expertise in pharmacogenomics, toxicogenomics, or pharmacogenetics will also be considered. Electronic submissions as pdf files are encouraged and should be submitted to mcbsearch@life.uiuc.edu. To ensure full consideration, applications should be received before December 1, 2004. Additional information may be found at www.life.uiuc.edu/mcb. *UIUC is an AA-EOE.*

Department of Physics

The Department of Physics invites applications for a full-time, tenure-track or tenured faculty position to begin August 16, 2005. The candidate will establish an independent research program in theoretical and computational biophysics, broadly defined, which will compliment existing research areas and add to the existing close collaborations between experimentalists and theorists in the department and elsewhere on campus. Applications received by October 15, 2004, will receive full consideration. The job description and application instructions can be found at www.physics.uiuc.edu/People/FacSearchBiophys.html. *UIUC is an AA-EOE.*

Department of Plant Biology

The Department of Plant Biology invites applications for a full-time, tenure-track faculty position to begin August 16, 2005. The ideal candidate will have a background in cellular and molecular genomics, experience in quantitative genetics in plants, and the ability to develop and implement statistical and informatics protocols to solve biological problems. The department has a particular interest in interactive responses of plants to biotic or abiotic stresses with anthropogenic changes in atmosphere, and has world-class facilities for research in this area. Closing date is December 6, 2004. Please submit your curriculum vita, statements of research and teaching, and names of three references to Plant Genomics Search Committee, School of Integrative Biology, University of Illinois, 286 Morrill Hall, 505 South Goodwin Ave., Urbana, IL 61801 (phone: (217)333.3044; fax: (217)244.1224; email: sib@life.uiuc.edu). For more information see www.life.uiuc.edu/sib. *UIUC is an AA-EOE.*

Department of Statistics

The Department of Statistics invites applications for one or more full-time, tenure-track assistant professor or tenured associate professor positions to begin August 16, 2005. Areas of emphasis include bioinformatics, computational statistics, high dimensional data analysis, image analysis, time series, stochastic modeling and advanced statistical theory and methods. Closing date is December 1, 2004. Applications with curriculum vitae, statement of research and teaching, three letters of recommendation, and (p)reprints should be sent to: Chair, Statistics Search, Department of Statistics, 725 South Wright St., 101 Illini Hall, Champaign, IL 61820 (phone: (217)333.2167; email: office@stat.uiuc.edu). For more information visit www.stat.uiuc.edu/jobs. *UIUC is an AA-EOE.*

COLLEGE OF AGRICULTURAL AND ENVIRONMENTAL SCIENCES
University of California, Davis

The College of Agricultural and Environmental Sciences is pleased to announce that we will be recruiting the following positions during 2004-05. Please refer to the websites listed below or at **http://provost.ucdavis.edu/cfusion/emppost/search.cfm** for additional information. We anticipate that active recruitment will be underway for all positions beginning fall 2004. All positions will remain open until filled.

Positions are nine-month tenure track appointments (unless otherwise indicated). Eleven-month term employment will be offered and continued based upon academic personnel review.

Assistant Professor/Plant Sciences: There are three faculty positions available for recruitment in the fall of 2004 in the Department of Plant Sciences. The disciplinary areas have yet to be identified. Please refer to **http://plantsciences.ucdavis.edu**/ for updated information.

Assistant Professor/Animal Science: Recruitment for two faculty positions in the Animal Science Department will begin in fall 2004. One position will be in the field of mammary gland biology; the disciplinary area for the second position has not yet been identified. Please refer to **http://animalscience.ucdavis.edu** for updated information.

Assistant Professor/Plant Pathology: There is a faculty position available for recruitment in the fall of 2004 in the Department of Plant Pathology. The disciplinary area has yet to be identified. Please refer to **http://www.plpnem.ucdavis.edu** for updated information.

Assistant Professor/Economics of Agriculture, Department of Agricultural and Resource Economics: Teach and conduct research concerning the economics of agriculture. Appropriate areas of specialization include agricultural finance, agricultural marketing, agricultural policy, agricultural production, environmental/natural resource economics, or international trade/development. Send applications to **Professor Jeffrey Williams, Search Committee Chair, e-mail: ARESearch@primal.ucdavis.edu**. To ensure consideration, apply by **November 30, 2004**.

Assistant Professor/Environmental or Natural Resource Economics, Departments of Agricultural and Resource Economics (70%) and Environmental Science and Policy (30%): Teach and conduct research in environmental economics or natural resource economics. Send applications to **Professor Jeffrey Williams, Search Committee Chair, e-mail: ARESearch@primal.ucdavis.edu**. To ensure consideration, apply by **November 30, 2004**.

Assistant Professor/Adult Development: Teach and conduct basic and applied research on adult development with a lifespan perspective concerned with issues of individual and/or family health and well-being. For information contact: **Rosemarie Kraft, Search Committee Chair, Department of Human and Community Development. Telephone: (530) 754-9446. E-mail: rhkraft@ucdavis.edu**. To ensure consideration, apply by **November 1, 2004**.

Assistant Professor/Human Development: Teach and conduct basic and applied research aimed at preventing one or more types of individual or family maladjustment or impairment. For information contact: **Rand Conger, Search Committee Chair, Department of Human and Community Development. Telephone: (530) 757-8454 E-mail: rdconger@ucdavis.edu**. To ensure consideration, apply by **November 1, 2004**.

Assistant Professor/Environmental Chemist: Teach and conduct research in fundamental and applied aspects of environmental chemistry. This position will be under recruitment in late summer/early fall. For additional information contact: **Marion Miller, Search Committee Chair, Department of Environmental Toxicology, e-mail mgmillersears@ucdavis.edu**.

Assistant Professor/Nutrition: Teach and conduct basic and quantitative research in nutrition, metabolism and cell biology. For information contact: **Bo Lonnerdal, Search Committee Chair, Department of Nutrition. Telephone: (530) 752-8347. E-mail: bllonnerdal@ucdavis.edu**.

Professorial positions have responsibilities for teaching, undergraduate and graduate student advising, university, public and professional service, outreach, and research. Research and outreach must contribute to the mission of the Agricultural Experiment Station. Candidates must have a Ph.D. in an appropriate field. Applicants should submit resume, transcripts (if within five years of graduation), statement of research and teaching experience, list and reprints of publications, and the names and addresses of at least three people familiar with the applicant's qualifications, to individual and department as noted for position (department name), **University of California, Davis, CA 95616**. Please indicate the position(s) in which you are interested.

The University of California is an Affirmative Action/Equal Opportunity Employer.

Faculty Positions

Department of Biochemical Science and Technology, Institute of Microbiology and Biochemistry

National Taiwan University

The Institute of Microbiology and Biochemistry and the Department of Biochemical Science and Technology at National Taiwan University invites applications for **three** tenure-track Assistant, Associate or Full Professor positions, for teaching and research in **Structure Biology**, **Microbiology** and **Biochemistry**, respectively.

We seek interactive individuals with the ability to establish and maintain a vigorous and creative independent research program and commitment to teaching at both the undergraduate and graduate levels. The successful candidate should hold a Ph.D. or equivalent degree in related fields.

Applicants should send curriculum vitae, a summary of research interests and teaching plan, publication list, certification of working experiences, graduate transcripts, photocopy of Ph.D. diploma, four copies of reprints of relevant publications (published after 2002 and highlight a representative paper in the application letter), three letters of reference to:

The Faculty Searching Committee,
College of Life Science
National Taiwan University,
1, Sec. 4, Roosevelt Road,
Taipei, Taiwan 106, by 31 October, 2004.

For more details, please see:
www.bst.ntu.edu.tw (structure biology),
www.mbc.ntu.edu.tw (microbiology, biochemistry)

Tenure-Track Assistant Professor

Stony Brook University's Department of Physiology and Biophysics in the School of Medicine invites applications for a tenure-track Assistant Professor position. Exceptional candidates at the Associate Professor level will also be considered. The successful candidate is expected to have or to establish an innovative externally funded research program in an area that builds on existing strengths within the department: cellular and molecular aspects of signal transduction, membrane biophysics, and systems biology. (For a description of departmental research activities, please visit *www.pnb.sunysb.edu*).

The position includes a generous start-up package. Support facilities include cores for cell imaging, transgenic mice, DNA sequencing, proteomics, microarray studies, molecular cloning, bioinformatics, and cell culture. The department also has access to the facilities at Brookhaven National Laboratory.

Required: Ph.D. and/or M.D. and postdoctoral research experience.

The priority deadline for applications is December 15, 2004.

To apply, please send a curriculum vitae, list of publications, description of research interests, and three letters of reference to: Search Committee Chair, Department of Physiology and Biophysics, Stony Brook University/SUNY Stony Brook, NY 11794-8661.

AA/EOE.
Visit *www.stonybrook.edu/cjo* for employment information.

STONY BROOK

FACULTY POSITION AT MIT DEPARTMENT OF BIOLOGY

The Massachusetts Institute of Technology Department of Biology is seeking an outstanding scientist for a tenure track position as an Assistant Professor. We are interested in candidates with important research contributions, the ability to develop a significant and independent research program, and a commitment to excellence in undergraduate and graduate education.

The applicant's research program should involve physiologic, genomic or other systems approaches to the study of cells or organisms or the interactions between cells or between organisms. Areas of interest include but are not limited to cell biology, developmental biology, neurobiology, and evolutionary biology.

Applicants should submit a curriculum vitae, a summary of current and proposed research programs, and should arrange for three letters of recommendation to be sent to:

Biology Search Committee
Attn: Dr. H. Robert Horvitz
MIT Room 68-132
77 Massachusetts Avenue
Cambridge, MA 02139

Consideration of completed applications will begin on **October 12, 2004**.

MIT is an Affirmative Action/Equal Opportunity Employer. Qualified women and minority candidates are especially encouraged to apply.

FACULTY POSITION IN THE DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY UNIVERSITY OF ARIZONA

The Department of Molecular and Cellular Biology (www.mcb.arizona.edu) is seeking a new tenure-track faculty member for appointment in 2005. Although an appointment at the assistant professor level is preferred, outstanding candidates at more senior levels will be considered. Applicants with research interests in any area of molecular, cellular, or developmental biology, including those pursuing mathematical and statistical approaches to biological problems, will be considered. Candidates with the potential for establishing strong ties with other University of Arizona investigators in areas such as neurobiology, cancer biology, systems biology, or computational biology will be favored. Successful candidates will be expected to establish a competitive research program and to teach at both the undergraduate and graduate levels. Send curriculum vitae, a 1-2 page statement of research and teaching interests, and have at least three supporting letters sent to: **Kathleen Dixon, Head, University of Arizona, Department of Molecular and Cellular Biology, 1007 E Lowell, Life Sciences South Building, Room 444, Tucson, AZ 85721, USA**. To ensure consideration, complete applications should be received by **October 15, 2004**, although applications will be accepted until the position is filled.

The University of Arizona is an EEO/AA Employer/M/W/D/V and is seeking individuals who are able to work with diverse students or colleagues, and who have experience with a variety of teaching methods and curricular perspectives.

WRIGHT STATE *UNIVERSITY*

Department of Biological Sciences Tenure-Track Faculty Positions

The **Department of Biological Sciences of Wright State University** invites applications for multiple tenure-track faculty positions at the level of **ASSISTANT** or **ASSOCIATE PROFESSOR**. We anticipate hiring 5–7 new faculty over the next 3 years. Successful candidates must have a doctorate by time of appointment and sufficient research experience to establish and maintain an independent, extramurally funded research program. Positions available include:

- **Bioeducator:** The successful candidate will share a joint appointment between the College of Science and Mathematics (two-thirds) and the College of Education (one-third). Teaching efforts will be directed at training pre-service early and middle childhood teachers and research into science education. The candidate will interact with other science educators who are contributing to WSU's unique interdisciplinary effort to enhance the teaching of science. A Ph. D or Ed. D and either a graduate degree in Biological Sciences or two years related experience in a biological field are required. Experience teaching at the pre-college level is preferred.
- **Cell/Molecular Biologist:** Preference will be given to candidates with research expertise in immunology, virology, neurobiology, signal transduction, bioinformatics/computational biology, or microscopy: Opportunities for departmental collaboration include current faculty research on cell cycle regulation, cytoskeletal dynamics, immune and inflammatory mechanisms, bioinformatics, molecular evolution, and microbiology.
- **Ecologist/Environmental Scientist:** Preference will be given to candidates with expertise in fish ecology, toxicology/toxicogenomics, or whose research interests bridge multiple scales (metapopulations, ecosystems, landscapes). Opportunities for departmental collaboration include current faculty research in aquatic biology, plant/woodland ecology, ecotoxicology, and environmental risk assessment.
- **Invertebrate Biologist:** The successful candidate should specialize in zoology, ecology, or evolution. Opportunities for departmental collaboration include current faculty research in plant-herbivore interactions, parasitology, aquatic biology, evolution, development, and comparative physiology.
- **Organismal/Exercise Physiologist:** The successful candidate will augment departmental research programs studying comparative animal, exercise, and plant physiology. Approaches from molecular to organismal are welcome. Candidates interested in being involved with the Exercise Biology program are encouraged to apply.

Competitive start-up packages will be tailored to the specific needs of successful candidates. Instructional responsibilities will include teaching undergraduate and graduate courses in the area of specialization and mentoring graduate students participating in the BioMedical Sciences Ph.D. program, the Environmental Sciences Ph.D. program, the Biological Sciences M.S. program and/or the Microbiology and Immunology M.S. program. Applications from couples who have independent research programs are invited.

WSU is a major metropolitan university with more than 15,000 undergraduate and graduate students. Biological research facilities/resources at WSU include a Genomics Core Facility; a modern animal care facility; a newly constructed green house; and on-campus wooded Biology Preserve. The department graduates approximately 150 students per year in programs that include general Biology, Clinical Laboratory Sciences, Exercise Biology and Environmental Health.

The Department of Biological Sciences and the College of Science and Mathematics are committed to initiatives that include under-represented groups in undergraduate and graduate education. It is hoped that one or more successful candidates will be able to recruit minority students to these initiatives.

Appointment at the Associate level will require meeting the criteria in the Department Bylaws. More information on WSU, the Department of Biological Sciences, its Graduate Programs, and this job search can be found at **http://biology.wright.edu/dept/jobs04.html**.

Send a curriculum vitae, statement of research and teaching interests, and names and contact information for three references to **Chair of the Search Committee, Department of Biological Sciences, Wright State University, Dayton, OH 45435-0001**. Electronic applications can be sent to **biology@wright.edu**. Indicate in your letter which area(s) of specialty you are applying for. Review of applicants for all positions will begin November 14, 2004 and continue until all positions are filled.

Wright State University is an Affirmative Action/Equal Employment Opportunity Employer.

Nanyang Technological University

Assistant/Associate Professor in Bioengineering

The life sciences and related industries in Singapore and Asia at large have seen tremendous growth in recent years. With the demand for trained engineers and researchers with knowledge interfacing life sciences and engineering, a new bioengineering program has been initiated at the Nanyang Technological University (NTU). Together with its predecessor Nanyang University, NTU has offered higher education since 1955. NTU boasts of a campus of 200 hectares, an academic staff strength of over 1,360 and an enrolment of 16,000 undergraduate students and 7,000 graduate students. Its research and infrastructure is very well-funded by the government and industries.

The Division of Bioengineering at NTU invites applications for tenure-track faculty appointments at the Assistant or Associate Professor level in all general areas of bioengineering including but not restricted to: tissue engineering, biomaterials, molecular and cellular mechanics, molecular bioengineering, bio-computing, bio-imaging and nano-biotechnology. Candidates should have a Ph.D. in relevant disciplines, preferably with postdoctoral experience and a strong publication record.

The newly formed Division under the College of Engineering attracts top undergraduate students in Singapore and regional countries, and will rapidly build up its graduate program. The well-funded Division will be equipped with state-of-the-art facilities for teaching and research, and it will be housed in a brand new building by 2006. The Division will have a core faculty and joint faculty appointments with other divisions/schools within NTU. Successful applicants can look forward to a research-stimulating environment and interaction with some of the best undergraduate and graduate students in Singapore and Asia.

Emoluments and General Terms & Conditions of Service

The commencing salary will depend on the candidate's qualifications, experience, and the level of appointment offered. Information on emoluments and general terms and conditions of service is available under the section on 'Terms and Conditions of Service for Academic Appointments' on the Office of Human Resources' website (http://www.ntu.edu.sg/personnel/terms.htm).

Application Procedure

To apply, please submit an application form (which can be downloaded from http://www.ntu.edu.sg/personnel/AppInforms.htm) or send a detailed curriculum vitae which should include your areas of research interest, list of publications and the names, postal and e-mail addresses of three referees. Applications should be sent to:

The Vice-President (Human Resources)
NANYANG TECHNOLOGICAL UNIVERSITY
Office of Human Resources
Administration Building, Level 4
50 Nanyang Avenue
Singapore 639798
Telefax: (65) 6791 9340
Email: rakinder@ntu.edu.sg

uOttawa
L'Université canadienne
Canada's university

The University of Ottawa and the National Research Council of Canada Institute for Biological Sciences (NRC-IBS) are joining forces to create a research institute focused on the innovative development and application of systems biology to neurological diseases and cancers. A fundamental principle of the institute is to foster a multidisciplinary research environment that includes academia, government and industry. The institute will: develop advanced technologies to interrogate cellular processes and apply these technologies to the understanding of diseases. Established leading scientists from the University of Ottawa and NRC-IBS are providing the scientific foundation of the institute. To foster the growth and development of this new Institute the Faculty of Medicine of the University of Ottawa is seeking to recruit up to five new tenure stream faculty and Canada Research Chairs. Both junior and senior candidates that are recognized leaders in one or more of the following areas are encouraged to apply: computational biology, genomics, proteomics, bioinformatics, structural biology, stroke and cancer research, analytical biochemistry, metabolomics and glycomics.

We invite interested applicants to send their resume, statement of research interests and activities, and the names and addresses of three references, to: **Dr Daniel Figeys C/O the Research Office, Faculty of Medicine, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, K1H 8M5, Canada. Email: sysbio@uottawa.ca**. We thank all applicants who apply. However, only those selected for an interview will be contacted.

All qualified candidates are encouraged to apply; however, Canadian citizens and permanent residents will be given priority. Equity is a University of Ottawa policy; women, aboriginal people, members of visible minorities and persons with disabilities are invited to apply.

Polytechnic University
Celebrating 150 Years

CBSE
Othmer Department of Chemical & Biological Sciences & Engineering

Biology Faculty Position
Polytechnic University

The Othmer Department of Chemical and Biological Sciences and Engineering (CBSE) of Polytechnic University invites applications for a tenure-track faculty position in Biological Sciences at the Assistant or Associate Professor level, to begin January 2005. Qualified candidates must have a PhD in Biology or a closely related field. The successful applicant will have a strong commitment to teaching biological sciences in a science/ engineering school environment, and will serve as Co-Director of the undergraduate pre-medicine program in Biomolecular Sciences. They will have a strong record of achievement in research, and will be expected to establish an independent, externally funded research program in molecular or structural biology, protein engineering or biocatalysis.

Qualified candidates should e-mail their vitae, one research paper selected by the candidate as his/her best work, graduate transcript, a list of three professional references, and a statement of teaching and research objectives to **Professor Mary Cowman (mcowman@poly.edu)**, Chairperson of the Faculty Search Committee. Letters of recommendation will be sought at a later time, upon mutual agreement. Polytechnic University, the second oldest technological university in the United States, is located in Brooklyn, New York, inside the Metro Tech Center, a 16-acre academic/research/commercial complex, just across the Brooklyn Bridge, minutes from Manhattan.

EOE/AA.

ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

The **Department of Natural Resources & Environmental Sciences (NRES) at the University of Illinois** has tenure track faculty positions available beginning in August 2005. NRES has faculty in biological, physical, and social sciences applied across the landscape in natural, forested, agricultural, and urban ecosystems (www.nres.uiuc.edu). Interdisciplinary and systems-based approaches are important elements of our research and education programs. NRES has programs in horticulture, forestry, soil and water, human-environment interactions, wildlife, and related sciences.

Asst/Assoc Prof. of Soil or Environmental Microbiology - Job #9366. Conduct research in microbial ecology, nutrient cycling and microbially regulated processes occurring in soil and water that sustain the productivity and the environmental function of Illinois' agriculture, industries and landscapes. Teach an upper division soil microbiology course and one or more graduate level courses in soil microbiology. Closing date to apply is **September 30, 2004**.

Asst/Assoc Prof. of Wildlife Ecology and Management - Job # 9367. Plan, develop, conduct, and supervise research on some aspect of wildlife ecology with applications to conservation and management issues. Research can address questions from the molecular to landscape scale. Teach one undergraduate course in wildlife ecology and at least one senior or graduate course in the person's area of expertise. Closing date to apply is **October 31, 2004.**

For a complete job listing including application information, please visit our web site at **http://www.nres.uiuc.edu/careers/nresjobs.html.**

Assistant/Associate/Full Professor of Laboratory Animal Pathology (tenure track). School of Veterinary Medicine, University of California, Davis. Veterinarian with advanced training in the pathology of laboratory animals, specifically genetically altered mice preferred. PhD or equivalent postdoctoral research training required at appointment. Board certification or eligibility in Veterinary Anatomic Pathology required. Demonstrated aptitude/experience in teaching. Documented research record or potential to develop an independent research program using contemporary pathology and molecular technologies for the characterization of disease pathogenesis using genetically altered mice preferred. Interest in developmental biology, infectious diseases, or tumor biology preferred. Potential and/or demonstrated ability in acquisition of extramural funding. Must possess excellent interpersonal and communication skills and a demonstrated ability to work with others in a collegial team atmosphere. To receive fullest consideration, applications must be received by **November 1, 2004**; position open until filled. Expanded position description at **http://www.vetmed.ucdavis.edu/pmi/**.

Submit letter of intent outlining special interest in the position, overall qualifications, experience, and career goals; CV; and names and addresses of three professional references to: **Dennis W. Wilson, Chairman, Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, CA 95616, Attn: Donna Roggenkamp**.

AA/EOE

National Research Council Canada | Conseil national de recherches Canada

Research in Neuroglycobiology and Glycoproteomics Institute for Biological Sciences Ottawa, Ontario, Canada

The National Research Council of Canada's Institute for Biological Sciences (NRC-IBS) is expanding activities in neuroglycobiology and glycoproteomics. This expansion is within the scope of the joint initiative with the University of Ottawa to create a research institute focused on the development and application of systems biology to neurological diseases and cancer. NRC-IBS has established expertise in prokaryotic glycobiology, neurobiology, genomics and proteomics (please refer to our web site http://ibs-isb.nrc-cnrc.gc.ca/ibs/). We are building on these capacities and seeking mid-career or senior scientists for continuing positions to establish programs and multidisciplinary teams in glycobiology of neural regeneration, regulation of inflammatory cell trafficking in the brain and blood-brain barrier mechanisms. To complement these activities, a position in mass spectroscopic techniques applied to glycoproteomics is also available. Applicants with expertise and established publication records in these areas are encouraged to apply. Joint or Adjunct appointments with the University of Ottawa will be encouraged.

We invite interested applicants to send their resume, statement of research interests and activities, and the names and addresses of three references, to
Email: hrb.ibscomp.ext@nrc-cnrc.gc.ca
Web :http://careers-carrieres.nrc-cnrc.gc.ca
The deadline for applications is 27 September 2004.
Reference number: 65-04-33.

NRC is committed to employment equity. We thank all those who apply, however, only those selected for further consideration will be contacted.

Vous pouvez obtenir ces renseignements en français.

NRC·CNRC

Canada

THE UNIVERSITY OF CALIFORNIA AT BERKELEY

Faculty Positions in Molecular and Cell Biology

The Department of Molecular and Cell Biology is seeking applications for four faculty positions. We seek candidates with Ph. D. and/or M.D. degrees who have a strong interest in undergraduate and graduate teaching and demonstrated excellence, originality and productivity in research. Applications should include a *curriculum vitae*; a list of publications; a brief description of research accomplishments; a statement of research objectives and teaching interests; and reprints of three most significant publications. Please arrange to have three letters of reference sent to the address below. Potential reviewers should be referred to the Statement of Confidentiality found at: **http://apo.chance.berkeley.edu/evalltr.html**. Applicants are expected to join the faculty July 1, 2005 or thereafter.

Division of Immunology (Search ID#916)

We seek candidates at any level (tenured or tenure-track). Excellent candidates in all areas of Immunology will be considered, but we are particularly interested in those working on host-pathogen interactions; pathogenesis; innate immunity; tumor immunology; cytokine signaling; inflammation; cancer biology and signal transduction. Closing date for receipt of applications is **November 15, 2004** but applicants are encouraged to apply early as interviews may begin before the closing date.

Applications should be sent to:
Chair, Immunology Search (#916)
Department of Molecular and Cell Biology
University of California at Berkeley
142 Life Sciences Addition #3200
Berkeley, CA 94720-3200

Division of Biochemistry and Molecular Biology (Search ID#918)

We seek applications for a faculty position at the level of Assistant Professor (tenure-track). Excellent candidates in all areas of modern biochemistry will be considered; we are particularly interested in candidates who are dissecting cellular processes by the reconstitution and analysis of cell-free reactions. Closing date for receipt of applications is **October 15, 2004**.

Applications should be sent to:
Chair, Biochemistry & Molecular Biology Search (#918)
Department of Molecular and Cell Biology
University of California at Berkeley
142 Life Sciences Addition #3200
Berkeley, CA 94720-3200

Division of Cell and Developmental Biology (Search ID#917) Mammalian Physiology, Development and Disease

We seek applications for a faculty position at the level of Assistant Professor (tenure-track) in any field within the general area of mammalian physiology, development and disease. Areas of particular interest include mammalian cell physiology; tissue and organ morphogenesis; stem cell biology; tumor biology; and mouse models of physiological regulation and disease. Closing date for receipt of applications is **November 1, 2004**.

Applications should be sent to:
Chair, Vertebrate Development & Physiology Search (#917)
Department of Molecular and Cell Biology
University of California at Berkeley
142 Life Sciences Addition #3200
Berkeley, CA 94720-3200

Division of Genetics & Development (Search ID#814) Vertebrate Developmental Genetics

We seek applications for a faculty position at the level of Assistant Professor (tenure-track). Candidates who apply genetic and embryological techniques to the study of vertebrate development and particularly to the mouse embryo are preferred. Closing date for receipt of applications is **November 1, 2004**.

Applications should be sent to:
Chair, Vertebrate Development & Physiology Search (#814)
Department of Molecular and Cell Biology
University of California at Berkeley
142 Life Sciences Addition #3200
Berkeley, CA 94720-3200

Applicants wishing to be considered for more than one position should submit a separate application to each Chair (a single application will suffice for the positions in Cell and Developmental Biology or Genetics and Development). All appointments are for 9-month positions and are subject to budgetary approval.

The University of California is an Affirmative Action/ Equal Opportunity Employer.

ALBERT-LUDWIGS-UNIVERSITÄT FREIBURG

The Institute of Microsystem Technology (IMTEK) in the Faculty of Applied Sciences at the University of Freiburg, Germany, is one of the largest European academic research departments active in the fields of microsystem technology and MEMS. Eighteen tenured faculty members, supported by an infrastructure including a 600 m² silicon fabrication facility and extensive laboratory resources, are engaged in all areas of microsystems research (**www.imtek.de**). The IMTEK is seeking to fill the position of a

Associate Professor W3 (formerly C3) of Biomicrotechnology

The successful candidate will be expected to establish a comprehensive research and teaching program in biomicrotechnology, especially in the area of interactions of biological cells with microsystems.

The University of Freiburg aims to increase the percentage of women in research and teaching, and therefore encourages female candidates meeting the above qualifications to apply. The position is nominally tenure-track whereby tenure is awarded following a 3-year evaluation period. In special cases, a tenured appointment is possible. The State of Baden-Württemberg intends to reform the pay schedule for professors by 1.1.2005. Professors employed after this date will be paid according to the revised salary scale.

Applications, including a curriculum vitae, publications list and statement of research interests should be sent by October 31, 2004 to the Dean of the Faculty of Applied Sciences, University of Freiburg, Georges-Köhler-Allee 101, D-79110 Freiburg, Germany (**www.faw.uni-freiburg.de**).

MGH 1811

Assistant Professor
Massachusetts General Hospital Cancer Center and Harvard Medical School

The Massachusetts General Hospital Cancer Center is seeking applications for two tenure track faculty positions at the level of Assistant Professor of Medicine at Harvard Medical School. The successful candidates will occupy cancer center laboratories in the newly constructed Charles River Plaza research facility, which will also house research centers in genetics, physiological genomics, stem cell biology and computational biology. We seek outstanding individuals, who wish to establish a strong cancer research program, with interests including, but not limited to, cancer biology, cancer genetics, genetic model organisms, signal transduction, and cell cycle checkpoints. Candidates must hold an M.D. and/or Ph.D. degree (or equivalent), have postdoctoral experience and a strong record of accomplishment in research. Applications from women and minority candidates are also strongly encouraged.

Candidates should submit a curriculum vitae including a full list of publications and a brief statement of research and teaching interests to the email address below. Four letters of reference should be mailed directly to the Search Committee.

Search Committee
c/o Carol Ann Hannan
MGH Cancer Center
13th Street, Building 149, Room 7204
Charlestown, MA 02129

Email: channan@partners.org

Applications must be received by **October 15, 2004**.

Massachusetts General Hospital and Harvard University uphold a commitment to Affirmative Action and Equal Opportunity.

MAYO CLINIC

To learn more about Mayo Clinic and Rochester, MN, please visit **www.mayoclinic.org**

Genomics Faculty Position

S. C. Johnson Genomics of Addiction Program, Mayo Clinic College of Medicine

Applicants for this position should submit a cover letter expressing their interest and qualifications and their curriculum vitae before October 15, 2004, by e-mail or regular mail to:

Dr. Eric D. Wieben
Chair, Basic Scientist Search Committee
Mayo Clinic College of Medicine
Guggenheim 1011A
Rochester, MN 55905
E-mail: wieben.eric@mayo.edu
Fax: (507) 284-9759

The Mayo Clinic College of Medicine (www.mayo.edu) in Rochester, Minnesota, is seeking a permanent-track faculty member with interests in the area of genomics of addiction. The successful candidate should be an outstanding molecular biologist with a strong record of research accomplishments and scholarship in defining genomic variability as it relates to risk for alcoholism. The individual will have the opportunity to work closely with basic and clinical scientists that engage in cutting edge research into the genetic basis of addiction. An ultimate goal is to apply this research to the development of innovative treatment modalities. The individual will be extensively involved in the activities of the Mayo Genomics Research Center, which is striving to better understand, diagnose, treat, and ultimately prevent disease through genomic technologies.

The Mayo Clinic S. C. Johnson Genomics of Addiction Program is a newly funded entity that expands upon the current Mayo Clinic commitment to research in genomic medicine. In addition to this position, three other senior scientists are being recruited to launch new research initiatives in the genomics of alcoholism. These additional recruitments are for a clinical psychiatric scientist, a bioinformatics researcher able to develop novel approaches to the analysis of the interactions of multiple vulnerability genes, and a genomic bioethicist.

Mayo Clinic is a not-for-profit organization that integrates research with clinical practice and education in a multi-campus environment. Rochester, Minnesota, is approximately one hour from the Minneapolis/St. Paul metropolitan area. To learn more about Mayo Clinic and Rochester, please visit www.mayoclinic.org. A competitive compensation and benefits package is available.

Mayo Foundation is an affirmative action and equal opportunity educator and employer. Post offer/pre-employment drug screening is required.

UMASS

University of Massachusetts Medical School
Department of Biochemistry and Molecular Pharmacology

BIOCHEMISTRY, BIOPHYSICS and CHEMICAL BIOLOGY

The Department of Biochemistry and Molecular Pharmacology is pleased to announce the continuing expansion of its faculty and facilities. We are seeking to fill several junior and/or senior level tenure track positions with candidates who utilize chemical, biochemical and biophysical techniques to address fundamental problems in biology. Innovative individuals with strong research accomplishments in synthetic, combinatorial, medicinal, and/or mechanistic organic chemistry are especially encouraged to apply, as are investigators who utilize NMR spectroscopy to address mechanistic or structural questions in biological systems. The department has established X-ray, NMR, Proteomics/Mass Spectroscopy, and Chemical Synthesis/Screening Facilities to support the research activities of its faculty.

The Department of Biochemistry and Molecular Pharmacology occupies two floors in a new 350,000 square foot research building that facilitates interactions with the neighboring Departments of Neurobiology, Cancer Biology, and Medicine and the Program in Gene Expression and Function. Salaries and start-up packages will be competitive and commensurate with accomplishment for both junior and senior applicants.

Junior applicants should send a cover letter explaining their interest in the department and a curriculum vitae that includes honors, publications and a brief research plan. Senior applicants should also include a brief description of current and future research activities and information on current grant support. Applicants should also provide the names and addresses of three individuals who are familiar with their work and potential for success. Applications will be reviewed expeditiously and interviews will begin in October. Materials should be sent to:

Reid Gilmore, Ph.D.
Chair, Faculty Search Committee
Department of Biochemistry and Molecular Pharmacology
The University of Massachusetts Medical School
Lazare Research Building
364 Plantation Street
Worcester, MA 01605

The Departmental web site is located at: **http://www.umassmed.edu/bmp/**

The University of Massachusetts is an Affirmative Action/Equal Opportunity Employer.

CATALYST BIOSCIENCES, INC.

Catalyst Biosciences is a dynamic Biotech start-up company that is developing a new therapeutic platform technology to create novel biopharmaceuticals that address large, unmet medical needs in the fields of inflammation and oncology. We are seeking talented, motivated professionals that will thrive in our highly productive, results-oriented, and collaborative culture.

Phage Display Scientist – This position requires significant experience with phage and/or other display technologies, including the construction of large libraries of protein variants and the use of multiple selection strategies. Previous experience with in vitro evolution of enzymes or antibodies and automated or semi-automated selection strategies is desirable, and experience with serine proteases and serine protease inhibitors is a plus. As our company grows, the successful applicant will assemble and lead a small phage display team. Managerial experience, particularly in a biotech environment, and the ability to excel both as an individual contributor and also as a member of an aggressive, dynamic team are important.

Protein Expression/Purification Scientist – We seek an outstanding scientist to lead a small protein expression/purification team. Experience with fermentation of Pichia pastoris and/or E.coli, purification of native proteins without added affinity tags, analytical biochemistry of proteins and proteomics technologies, and enzyme assays is highly desirable. Experience with serine proteases or metalloproteases and with automation of protein expression/purification or enzyme assays is a plus. Managerial experience, particularly in a biotech environment, and the ability to excel both as an individual contributor and also as a member of an aggressive, dynamic team are important.

Protein Expression/Purification Associate – We seek an experienced, motivated associate with significant experience in protein expression and purification. Significant experience with preparation of expression vectors, screening of expression strains, FPLC, PAGE, and enzyme assays is desired. Experience with automation of protein expression/purification or enzyme assays is a plus.

Automation Scientist – We seek an exceptional scientist or engineer with substantial experience establishing automation of biochemical and molecular biological protocols such as enzyme assays, protein expression/purification, phage display, PCR, mutagenesis, and colony screening. Previous experience in a biotech environment and familiarity with enzymes are desired.

Discovery Informatics Scientist – We seek a highly qualified individual who will excel in a start-up environment and build and/or manage relational databases and proprietary databases containing biochemical and molecular biological information. The successful applicant will also utilize our extensive, proprietary structure/function data to design and test predictive algorithms for an important class of protein therapeutic agents. The successful applicant will also manage the company's interactions with external IT professionals.

Director, Pharmacology – The successful applicant will report to our VP, Research and will assemble and lead a small pharmacology group that will test a new class of protein therapeutic agents in angiogenesis, oncology, and inflammation models. Experience establishing and utilizing models in these three therapeutic areas, contributing in a biotech or pharmaceutical environment, and leading teams of at least 3-4 pharmacologists is required.

Please send cover letter and resume to: **Catalyst Biosciences, Inc., 225 Gateway Boulevard, South San Francisco, CA, 94080; email: jobs@catbio.com**.

Catalyst is an Equal Opportunity Employer with competitive compensation and benefits, including equity participation in our pre-IPO company.

The University of Texas M. D. Anderson Cancer Center Faculty Position in Developmental Biology and Cancer

The Department of Biochemistry and Molecular Biology at **The University of Texas M. D. Anderson Cancer Center** is seeking applications from outstanding scientists for a tenure track faculty position in the area of developmental biology and cancer. Applications are encouraged from those individuals using genetic approaches in model organisms to study problems of cell biology and differentiation, chromatin organization and gene regulation, organ and tissue development, and/or signal transduction as they relate to cancer. We offer a highly attractive recruitment package that includes laboratory and office space in the new Mitchell Basic Sciences Research Building, an active graduate and postdoctoral training program, and the unmatched scientific environment of the Texas Medical Center. Applicants should hold a Ph.D. and/or M.D. degree and be able to demonstrate their potential as independent scientists. Those interested should send their C.V., a two-page research summary, and the names and addresses of at least three references before November 1, 2004, to: **Robert A. Schulz, Ph.D. Chair, Faculty Search Committee, Department of Biochemistry and Molecular Biology, Box 117, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, USA E-mail: raschulz@mdanderson.org**.

Department website:
www.mdanderson.org/DEPARTMENTS/biochem/

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Making Cancer History®

M. D. Anderson Cancer Center is an EOE employer and does not discriminate on the basis of race, color, national origin, gender, sexual orientation, age, religion, disability or veteran status, except where such distinction is required by law. All positions at M. D. Anderson are considered security sensitive; drug screening and thorough background checks will be conducted. The University of Texas M. D. Anderson Cancer Center values diversity in its broadest sense. Diversity works at M. D. Anderson. Smoke-free environment.

5 FACULTY POSITIONS AT THE BRAIN RESEARCH CENTRE

University of BC & Vancouver Coastal Health

The Brain Research Centre of UBC and Vancouver Coastal Health is embarking on a major expansion of its programs, based on recent successes in attracting substantial infrastructure funding. We have available 5 full-time tenured or tenure-track faculty positions, at both senior and junior levels, across a broad spectrum of areas in Neuroscience.

Applications are invited in the areas of **Stroke, Mood Disorders, Neuroprotection, Neurodegenerative Disorders, Postnatal Brain Development, Neuronal Plasticity, Synaptic Mechanisms, Cell Signaling**, and **Cognitive Neuroscience**. The Centre specifically encourages individuals using **brain imaging** and/or **genomic/proteomic** strategies to apply. The expected start date for these appointments is July 1, 2005 or 2006. The minimum salary for Assistant Professor is $75,000, but the salary will be negotiated and commensurate with qualifications and experience.

The University of British Columbia hires on the basis of merit and it is committed to employment equity. We encourage all qualified persons to apply; however, Canadians and permanent residents of Canada will be given priority. Applicants should submit a curriculum vitae, a statement of current research interests and future plans, and arrange for three (3) letters of reference to be submitted independently.

Apply to: **Dr. Max Cynader, Director, Brain Research Centre, University of British Columbia and Vancouver Coastal Health, 2211 Wesbrook Mall, Vancouver, BC V6T 2B5 Canada. Fax: (604) 822-0361 Email: info@brain.ubc.ca. Deadline for applications is November 1, 2004**

UBC Brain Research Centre

Vancouver Coastal Health

National Institute of Diabetes & Digestive & Kidney Diseases

Department of Health and Human Services
National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases

POSTDOCTORAL FELLOWSHIPS IN MOLECULAR AND CELL BIOLOGY AT THE NIH

Postdoctoral Fellowships are available in the Genetics and Biochemistry Branch, NIDDK, NIH. The Branch is similar to a small academic department and has excellent laboratory facilities. The intramural program of the NIH offers an outstanding research environment. The Branch is located on the main intramural campus of the NIH in Bethesda, Maryland, a 20-minute ride from Washington, D.C. Applications are invited from individuals of the highest caliber with Ph.D., M.D., or M.D., Ph.D. degrees. Physicians may participate in either the NIH Inter-institute Endocrine or the NIH Inter-institute Medical Genetics Training Programs. Current research interests of the staff include:

Protein targeting and translocation. Our group uses a combination of biochemical, genetic and cell biological methods to study mechanisms of protein targeting to the secretory pathway in eukaryotes and prokaryotes as well as mechanisms of protein translocation across the ER and bacterial inner membrane. For recent work see Proc. Nat. Acad. Sci. (2001) **98:** 3471, EMBO J. (2001) **20:** 6724, J. Biol. Chem. (2002) **277:** 43527, and J. Biol. Chem (2003) **278:** 46155. **(Harris Bernstein: harris_bernstein@nih.gov)**

Biochemistry and molecular biology of double-strand break repair and homologous recombination in eukaryotes and prokaryotes. Current interests include mouse meiosis (Mol. Cell (2000) **6:**975; Dev Cell (2003) **4**, 497), DNA damage and repair (Genes and Dev (2001) **15:** 415; Mol. Microbiol. (2002) **44**, 89), evolutionary genomics, with a particular emphasis on the evolution of sex chromosomes (Nature Genetics (2004) **36**, 642) and small molecule analogs of repair and recombination proteins, such as miniRecAs (Science (1996) **272:**868)). Approaches used include protein and peptide biochemistry, mouse knockouts, chromosome immunolocalization, structural biology, DNA microarrays, genomics, proteomics, and biophysical approaches. **(Dan Camerini-Otero)**

Molecular Mechanisms of DNA Repair. The lab's focus is on molecular and cellular studies of DNA mismatch repair proteins including their roles in DNA damage signaling, activation of cell cycle and checkpoint controls in mammalian cells, and the role of mismatch repair proteins in homologous recombination and meiosis. Approaches include biochemistry, structural biology, cell biology, and molecular genetics. [Nature (2000) **407:**703; J. Biol. Chem. (2001) **276:**28291; J. Mol. Biol. (2003) **334:**949; Proc. Natl. Acad. Sci. (2003) **100:**14822]. **(Peggy Hsieh: ph52x@nih.gov)**

Interested candidates should send a letter stating their interests, their curriculum vitae and list of publications, and arrange to have letters from three references sent to one of the investigators above or to **Dr. R. Daniel Camerini-Otero (camerini@ncifcrf.gov), Chief, Genetics and Biochemistry Branch at:**

Genetics and Biochemistry Branch
Bldg. 5, Rm 201
5 Memorial Dr MSC 0538
National Institutes of Health
Bethesda, MD 20892-0538

HHS and NIH are Equal Opportunity Employers

University of California, Berkeley: Pending budgetary approval, the Department of Psychology and the Helen Wills Neuroscience Institute invites applications for a 100% tenure-track position at the ASSISTANT PROFESSOR level in developmental neuroscience. The proposed start date is July 1, 2005. This position is a joint appointment (50%/50%) with the Department of Psychology and the Helen Wills Neuroscience Institute. Applicants should hold a doctoral degree in Psychology, Neuroscience, Cognitive Neuroscience or a related field. We are particularly interested in candidates employing neuroimaging techniques to study child development or childhood psychopathology (i.e., autism, ADHD).

Applications must be postmarked by **November 1, 2004**, and should include a resume, selected publications, and a brief statement of research interests and future plans sent to: **Neuroscience Search Committee, Helen Wills Neuroscience Institute, 132 Barker Hall, MC 3190, University of California, Berkeley, CA 94720-3190**. Candidates should also arrange to have at least three letters of recommendation sent to the same address and to request that referees read the University's statement on confidentiality (**http://apo.chance.berkeley.edu/evalltr.html**) prior to submitting their letters. Applications postmarked after **November 1, 2004**, cannot be considered. Review of completed applications will begin **October 15, 2004**.

The University of California is an Equal Opportunity/Affirmative Action Employer. All qualified applicants including minorities and women are encouraged to apply.

CHAIR, DEPARTMENT OF CELL AND DEVELOPMENTAL BIOLOGY

Upstate Medical University is seeking an energetic and highly motivated individual to assume the position of Chair of the Department of Cell and Developmental Biology.

The Department of Cell and Developmental Biology is one of five basic science departments. There are currently 14 full time members with $2 Million in externally funded research. Areas of research include signal transduction, cytoskeletal structure, cell motility, adhesion, angiogenesis, and neural development and repair. The Department also plays a critical role in the educational program of the College of Medicine and the College of Graduate Studies. The Chair will be responsible for setting the goals and objectives for the Department with an emphasis on enhancing the research portfolio through the recruitment of additional faculty.

Upstate Medical University is comprised of the Colleges of Medicine, Graduate Studies, Nursing, Health Professions, and the University Hospital. The annual budget is over $650 million. The College of Medicine is the 14th oldest in the country. It has a student enrollment of about 640 with an entering class of 160. There are 130 students pursuing degrees in the College of Graduate Studies. There are 445 faculty members, 65 of whom are in the basic sciences.

The Chair will report to the Executive Vice President and Dean, Steven J. Scheinman, MD.

The successful candidate will possess a doctoral degree in biomedical science; will be an internationally recognized investigator with substantial external research funding; have a record of scholarship that would qualify for a tenured Professorial appointment; and be able to mentor faculty and students.

For information on the University, see: www.upstate.edu

For additional information or to submit a CV, please contact in confidence:

Harry Wollman, MD, Principal or Raymond Alexander, Principal
Alexander, Wollman & Stark
1835 Market Street, Suite 1140
Philadelphia, PA 19103

E mail: alexwollstark@aol.com

Tel: 267-256-0721

Review of applications will be considered until the position is filled. Applications from women and minority candidates are especially welcome.

State University of New York
Upstate Medical University
Formerly known as SUNY Health Science Center

An AA/EEO/ADA employer, committed to excellence through diversity.

UNIVERSITÄT BAYREUTH

As part of the newly established *elite study program in Macromolecular Science* within the **Elite Network of Bavaria**, the University Bayreuth is seeking candidates for two faculty positions.

Applied Functional Polymers

at the Associate Professor level (W2)

The position is aimed to support the research activities in Macromolecular Chemistry and Experimental Physics and should further strengthen the interdisciplinary research focus on Polymer and Colloidal Science at the University Bayreuth. Applicants must have an outstanding research record in the development of organic electrooptical devices. They must have a strong commitment to teaching excellence within the elite study program in Macromolecular Science and in polymer chemistry or polymer physics at the undergraduate and graduate level.

Polymer Catalysis

at the Associate Professor level (W2)

This position is aimed to function as bridge between Inorganic Chemistry and Macromolecular Chemistry and should support the interdisciplinary research focus on Polymer and Colloidal Science. Applicants must have an outstanding research record in the development of modern catalysts for polymer synthesis, and must have a strong commitment to teaching excellence within the elite study program in Macromolecular Science and in inorganic and macromolecular chemistry at the undergraduate and graduate level.

The positions currently have a limited duration until September 30, 2009. A permanent position at the W2 level may be possible depending on achievements and availability of the position. **The daedline for applications is October 15, 2004**. Applications, supplied with curriculum vitae, list of publications, statement of research plans and teaching prospectus, together with full contact information (address, phone, fax and email) and three references should be sent to: **Faculty of Biology, Chemistry and Geological Sciences, Professor Dr. Ortwin Meyer, Dean, University Bayreuth, Universitätsstrasse 30, D-95440 Bayreuth, Germany.**

For more information, contact Professor Hans-Werner Schmidt at 0049 921 / 55 - 32 00 or at hans-werner.schmidt@uni-bayreuth.de.

FACULTY POSITION IN BEHAVIORAL ECOLOGY

Department of Biological Sciences
Dartmouth College

The Department of Biological Sciences at Dartmouth College seeks a **tenure track Assistant Professor in behavioral ecology**. We seek scientists testing hypotheses of general significance in rigorous, field-based studies. We define behavioral ecology broadly, but are particularly interested in researchers who link behavior to population level processes, especially evolution. Research with vertebrates is a plus. We seek an outstanding ecologist who will establish a vigorous research program and teach courses in animal behavior, ecology, and evolution at the undergraduate and graduate levels.

Submit a curriculum vitae, statements of research and teaching interests, and three letters of recommendation to: **Ecology Search Committee, Department of Biological Sciences, Dartmouth College, Hanover, NH 03755-3576.**

Although materials can be initially submitted by FAX (**603-646-1347**), original documents are required. Application review will begin on **October 15, 2004** and continue until the position is filled. For further information about the department and graduate programs, see **http://www.dartmouth.edu/~biology/**.

Women and members of minority groups are strongly encouraged to apply. Dartmouth College is an Equal Opportunity/Affirmative Action Employer.

PENNSTATE Altoona

BIOLOGY

(Tenure-Track)

The Pennsylvania State University, the Altoona College invites applications for a tenure-track position in Vertebrate Physiology in the Division of Mathematics and Natural Sciences, beginning in Fall 2005. The position requires a Ph.D. in Biology or a closely related discipline. Teaching duties will include introductory biology, mammalian anatomy for allied health students, upper-level vertebrate physiology (lecture/laboratory), and a course in his/her area of expertise. The successful candidate should contribute to our new baccalaureate program in Biology.

Only 40 miles from the University Park campus, Altoona College offers the advantages of small college teaching with the readily available resources of a major research university. Applicants should present a record of evidence and potential effectiveness in teaching, research, and service. Penn State Altoona offers a competitive salary and an attractive benefits package.

Applicants should send a letter of application establishing their qualifications; a current vita; a description of teaching philosophy and evidence of teaching effectiveness; a statement of research interests; transcripts (official transcripts required at the time of an interview); and a minimum of three letters of reference. Applicants are strongly encouraged to submit their applications and accompanying materials electronically to academicaffairs@psu.edu in Word or PDF formats. Review of applications will begin the week of November 1, 2004, and continue until the position is filled. Non-electronic inquiries, applications, and additional materials should be sent to: Chair Search Committee for Biology, Penn State Altoona, Box S-17972, 3000 Ivyside Park, Altoona, PA 16601-3760. For additional information about Penn State Altoona, please visit our web page at http://www.aa.psu.edu.

Penn State is committed to affirmative action, equal opportunity and the diversity of its workforce.

PENN STATE ***Making Life Better***

FACULTY POSITION
YALE UNIVERSITY
DEPARTMENT OF MOLECULAR BIOPHYSICS AND BIOCHEMISTRY

The Department of Molecular Biophysics and Biochemistry at Yale University seeks applicants for a faculty position in the broad area of molecular biophysics. Potential research areas include structural biology, spectroscopy and single molecule studies. Primarily, we seek to make an appointment at the Assistant Professor level, however more senior candidates with outstanding research accomplishments will also be considered. Our department, which is located in both the Faculty of Arts & Sciences and the School of Medicine of the University, spans a broad range of areas including biochemistry, biophysical chemistry, structural biology, molecular biology and molecular genetics.

Applications should include a curriculum vitae, a statement of research interests, three letters of reference, and reprints or preprints. Completed applications should be sent to: **Search Chair, Faculty Search Committee, Department of Molecular Biophysics and Biochemistry, Yale University, 260 Whitney Avenue, P.O. Box 208114, New Haven, Connecticut 06520-8114; Telephone: (203) 432-5593.** Application Deadline: **October 31, 2004**.

Yale is an Affirmative Action/Equal Opportunity Employer. Women and minorities are strongly encouraged to apply.

NUS National University of Singapore

Department *of* Biological Sciences
Faculty of Science

Faculty Search

The Department of Biological Sciences, National University of Singapore (NUS) invites applications for tenure-track faculty positions at Assistant Professorship and Associate Professorship levels.
Established in 1905, NUS has evolved into a quality teaching and research-intensive institution, which is internationally acknowledged as one of the finest universities in the Asia-Pacific. We are the largest life sciences department in NUS and have established state-of-the-art research facilities for structural biology, functional genomics, developmental biology and biodiversity. Faculty members can expect competitive salary levels and comparative research support as at the top universities in USA and Europe.
Preference will be given to applicants who specialize in the following areas:

1. Developmental biology of model organisms
2. Marine ecology and biodiversity
3. Structural biology and functional genomics, including cryoelectron microscopy
4. Chemical biology
5. Computational biology

Outstanding individuals with postdoctoral experience and strong commitment to research and teaching are encouraged to send an application (form downloadable from www.dbs.nus.edu.sg), along with curriculum vitae, a brief research plan and names of three external referees to:

Professor Choy-L HEW
Head, Department of Biological Sciences,
National University of Singapore
14 Science Drive 4
Singapore 117543
Republic of Singapore
Fax: (65) 67795671
Email: dbshead@nus.edu.sg

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Faculty Positions in Chemistry

at the Swiss Federal Institute of Technology Lausanne (EPFL)

The EPFL anticipates making several appointments at the level of tenure track Assistant Professor over the next few years in its Institute of Chemical Sciences and Engineering (ISIC).

We seek outstanding scientists with recognized accomplishments in any field of chemistry.

Exceptional candidates seeking a higher-level appointment may also be considered. The successful candidate will establish and lead a vigorous, independent research program, interact with existing projects and be committed to excellence in teaching at both the undergraduate and graduate levels. Significant start-up resources and research infrastructure will be available.

Applications with curriculum vitae, publication list, concise statement of research and teaching interests as well as the names and addresses (including email) of at least five references should be sent by **October 15, 2004,** to:

Professor Thomas Rizzo,
Head of the search committee
Institute of Chemical Sciences and Engineering
Faculty of Basic Sciences
EPFL
CH-1015 Lausanne, Switzerland

For additional information, please consult: http://www.epfl.ch, http://sb.epfl.ch and http://isic.epfl.ch

The EPFL is an equal opportunity employer.

THE AMERICAN UNIVERSITY IN CAIRO

FACULTY POSITIONS

Founded in 1919, AUC's campus is located in Cairo, Egypt, and its degree programs are accredited by the Commission on Higher Education of the Middle States Association of Colleges and Schools. For more information see our website at www.aucegypt.edu. The Ph.D. is required. University teaching experience is preferred. One- two- or three-year appointments subject to mutual agreement will begin September 2004. Renewal of an appointment depends upon institutional needs and/or the appointee's performance. The normal teaching load is three courses per semester and English is the language of instruction. Salary and rank are according to scale based on qualifications and professional experience. For expatriates, benefits include housing, annual round-trip air travel for appointee and qualifying dependents, plus schooling for the equivalent of up to two children at Cairo American College. In view of AUC's protocol agreement with the Egyptian Government, which requires specific proportions of Egyptian, U.S., and third-country citizen faculty, at this time preference will be given to qualified applicants who are U.S. citizens.

Department of Biology

The Department of Biology anticipates two openings. We are seeking biologists dedicated to teaching and research in a strong biology program within a liberal arts and sciences context. Successful candidates must teach all levels of undergraduate biology, including introductory courses for non-majors, and should be able to participate in research involving undergraduate students. Particular consideration will be given to candidates with strong background in molecular biology and in microbiology. **Position # BIOL 1/2**

Department of Electronics Engineering

The Department of Electronics Engineering anticipates one opening. The successful candidate will be expected to teach undergraduate courses in communication systems as well as introductory courses. Participation in research is expected. **Position # EE-1**

Department of Computer Science

The CSAB-accredited Department of Computer Science anticipates two openings. Successful candidates will teach upper division undergraduate and graduate Computer Science courses preferably in the areas of (a) Computer Graphics and Multimedia Systems; (b) Programming Languages. **Position # CS-1/2**

Department of Mathematics

The Department of Mathematics anticipates one vacancy. Successful candidate will teach all levels of undergraduate mathematics and statistics courses, as well as participate in research. **Position # MATH-1**

Department of Physics

The Department of Physics anticipates two openings. We are seeking physicists dedicated to teaching and research in a strong physics program within a liberal arts and sciences context. Successful candidates must teach at all levels of undergraduate and graduate physics and should be able to participate in research involving graduate students. Particular consideration will be given to candidates with strong background in instrumentation, nanotechnology, advanced materials and with laboratories. **Position # PHYS-1/2**

APPLICATION INSTRUCTIONS: E-mail a letter of application specifying **Position #** and attach a current C.V. and names and addresses of three references to **facultyaffairs@aucnyo.edu** or mail to:

Dr. Earl (Tim) Sullivan, Provost
The American University in Cairo
420 Fifth Avenue, Fl. 3
New York, N.Y. 10018-2729

For full consideration, candidates must complete the Personnel Information Form provided at **http://forms.aucegypt.edu/provost/pif3.html**.

Applications accepted until position is filled.
Formal review of applicants will begin November 1, 2004.

The American University in Cairo is an equal opportunity employer.

ASSISTANT PROFESSOR
MICROBIOLOGY

The Section of Microbiology (Division of Biological Sciences) at University of California, Davis, invites applications for a tenure-track position at the rank of Assistant Professor. This is a broadly based search for candidates working on tractable bacterial, archaeal or eukaryotic systems. Preference, however, will be given to candidates working in either of two areas – (1) bacterial pathogenesis with emphasis either on mechanisms of host-pathogen interaction or genetic adaptation of pathogen to the host or (2) genome analysis and its application to processes of bacterial evolution and function. Important qualifications are a creative intellect and an interest in interacting with a faculty working on both yeast and bacteria.

A PhD (or equivalent) degree is required and postdoctoral experience is recommended. The successful candidate will be expected to teach and advise both undergraduate and graduate students and to develop an original productive research program.

Applicants should submit a current curriculum vitae, copies of no more than five published (or in-press) papers and a statement including a plan of research to be initiated and teaching interests. Arrange for recommendation letters to be sent separately. Direct all information to: **Mitch Singer, Chair, Search Committee, Section of Microbiology, University of California, Davis, One Shields Avenue, Davis, CA 95616-8665.** While applications will be reviewed until the position is filled, only applications received by November 5, 2004 will be assured full consideration.

The University of California is an Equal Opportunity/ Affirmative Action Employer with a strong institutional commitment to the development of a climate that supports equality of opportunity and a respect for difference.

MAYO CLINIC

Physician Scientist Faculty Position

Rochester, Minnesota

The Department of Medicine at Mayo Clinic in Rochester, MN invites applications from persons interested in conducting patient or disease oriented research in support of cross-disciplinary research programs. Successful applicants will have an established extramurally funded research program and will receive substantial intramural support. Areas of research focus of particular interest include Aging, Clinical Immunology and Immunotherapeutics, Complementary and Integrative Medicine, Translational Immunovirology and Biodefense, Cancer or Molecular Medicine.

The successful candidate will have an MD, Ph.D. or an MD/Ph.D. degree(s) and must be eligible for hire at Mayo.

To learn more about Mayo Clinic and Rochester, MN, please visit **www.mayoclinic.org**

Interested applicants should submit a curriculum vitae, a statement of research interests and goals, along with the name of three references by November 1, 2004, to:

Vicente Torres, MD
Chair, Search Committee
Eisenberg Building S24

Mayo Clinic College of Medicine
200 First Street SW
Rochester, MN 55905

Mayo Foundation is an affirmative action and equal opportunity educator and employer. Post offer/pre-employment drug screening is required.

Assistant/Associate Professor, Comparative Pathology (50% tenure track, UC Davis), Assistant/Associate Professor In Residence (50% Animal Care Program, UC San Diego). This appointment in the Departments of Pathology, School of Medicine, UCSD and Pathology, Microbiology and Immunology (PMI), School of Veterinary Medicine, UC Davis will be **located at the University of California, Veterinary Medical Center - San Diego** (UC VMC-SD), a joint venture of UC Davis, and UCSD. Veterinarian with advanced training in anatomic pathology. Experience with mouse pathology preferred. PhD or equivalent postdoctoral research training required at appointment. Board certification or training sufficient to qualify for examination in Veterinary Anatomic Pathology. ACVP board certification preferred. Demonstrated aptitude/experience in teaching. Documented research record or potential to develop an independent research program using contemporary pathology and molecular technologies for the characterization of disease pathogenesis. Potential and/or demonstrated ability in acquisition of extramural funding. Must possess excellent interpersonal and communication skills and a demonstrated ability to work with others in a collegial team atmosphere. To receive fullest consideration, applications must be received by **November 1, 2004**; position open until filled. Expanded position description at **http://www.vetmed.ucdavis.edu/pmi/**.

Submit letter of intent outlining special interest in the position, overall qualifications, experience, and career goals; CV; and names and addresses of three professional references to:

Dennis W. Wilson, Chairman
Department of Pathology, Microbiology and Immunology
School of Veterinary Medicine
University of California
Davis, CA 95616
Attn: Donna Roggenkamp

AA/EOE

Cancer Biology Faculty Position

Stony Brook University's Department of Molecular Genetics and Microbiology in the School of Medicine invites applications for a tenure-track faculty position at the Assistant Professor level in the field of Cancer Biology.

Successful candidates will be expected to establish a vigorous extramural research program, direct graduate student and postdoctoral research, and participate in departmental teaching and administrative responsibilities. The Department of Molecular Genetics and Microbiology and Stony Brook University provide a highly interactive scientific community with world-class research facilities. The Department has training grants to support graduate students and postdoctoral fellows. The School of Medicine and University maintain core facilities that include imaging, sequencing, animal/transgenic, cell sorting, proteomics, microarray, bioinformatics, and cell culture.

Applicants must have a Ph.D., M.D., or M.D./Ph.D. and have at least two years of postdoctoral experience. Outstanding candidates whose research is in the area of cancer biology are encouraged to apply. Specific areas of interest include, but are not limited to, signal transduction, tumor-host interactions, cancer genetics, and stem cell biology. Special consideration will be given to candidates involved in translational research and whose research complements existing areas of expertise within the Department.

Applications for this position must be received no later than December 31, 2004. Review of applications will begin November 1, 2004, and continue until December 31, 2004, or until the position is filled. Recruitment will begin in Fall 2004, with a tentative start date of June 2005.

Candidates should send a CV, two representative publications, a brief summary of accomplishments and future research interests (maximum 3-4 pages), and the names and contact information of three references to:

Patrick Hearing, Ph.D., Chair of Search Committee
Department of Molecular Genetics and Microbiology
130 Life Sciences, Stony Brook University
Stony Brook, NY 11794-5222

AA/EOE. Visit *www.stonybrook.edu/cjo* for employment information.

STONY BROOK

FACULTY POSITIONS IN DEPARTMENT OF CELL BIOLOGY

The Department of Cell Biology invites applications for several tenure-track positions. Candidates must have a strong record of achievement and a well-formulated and innovative research plan.

Most positions will be at the Assistant Professor level, but outstanding candidates at other levels will be considered. Preference will be given to areas that complement existing strengths in molecular cell biology, signaling and development, with a focus on stem cells and organogenesis (see www.cellbio.duke.edu). We are also seeking candidates working on nuclear/chromatin structure, cell polarity, and models of human physiology and disease.

The Department is in a major expansion phase and successful applicants will enjoy newly renovated space, and a stimulating and supportive research environment. Applications will be considered as they are received, up to October 30th 2004.

Please include CV, brief summary of past and future research, and reprints of recent papers, and arrange for three letters of support to be sent directly to: **Dr. Brigid LM Hogan, Chair, Department of Cell Biology, Room 388C, Nanaline H. Duke Building, Box 3709, Duke University Medical Center, Durham, NC 27710.**

Duke University Medical Center

Duke University Is An Equal Opportunity/Affirmative Action Employer

TENURE TRACK FACULTY POSITIONS IN BIOCHEMISTRY

PURDUE UNIVERSITY

The Department of Biochemistry seeks to hire multiple individuals who will develop nationally and internationally recognized research programs, interact with scientifically diverse faculty across campus and demonstrate excellence in teaching. Scientists investigating biochemistry relevant to eukaryotic organisms in the following areas will be given preference.

- Post-transcriptional gene regulation. Examples include, but are not limited to RNA splicing, RNA processing, RNA interference, and regulation of translation.
- Signal transduction. Areas related to the cell cycle, cancer and metabolic regulation are of particular interest.
- Plant biochemistry. Applicants studying plant growth regulators or metabolism are strongly encouraged to apply.

We are particularly interested in applicants using biophysical approaches or chemical biology to explore these problems. The department is part of a large and vibrant life science community at Purdue, and our faculty participate in interdisciplinary programs in biochemistry and molecular biology, biophysics, genetics, plant biology, and neuroscience. Support facilities for DNA and protein sequence analysis, mass spectrometry, NMR, X-ray crystallography, image analysis, computation, and transgenic animal work are available. For more information about our department, see **www.biochem.purdue.edu**.

Applicants should have a Ph.D., a strong publication record, at least two years of post-doctoral experience or its equivalent, the potential to develop a vigorous extramurally funded research program, and a commitment to research and teaching excellence. Appointments at Assistant Professor, Associate Professor or senior rank will be considered. To apply, send curriculum vitae, a two-page summary of research interests, and a statement of teaching interests to: **Biochemistry Search Committee, Department of Biochemistry, 175 S. University Street, West Lafayette, IN 47907-2063, USA.**

The applicant should request that three individuals familiar with the applicant's work send letters to the above address and the application should include the names and contact information for each of those three persons.

Electronic applications are welcome and may be sent to: **biochem-search@purdue.edu**, with a hard copy application also being sent to the above address. Screening of applicants will begin immediately and continue until the positions are filled.

Purdue University is an Equal Opportunity/Equal Access/Affirmative Action Employer fully committed to achieving a diverse workforce. Women and minority applicants are encouraged to apply.

FACULTY POSITION CELL BIOLOGY

The Department of Biological Sciences at Vanderbilt University seeks candidates to fill a tenure-track faculty position in cell biology. We are especially interested in candidates studying topics such as protein trafficking, cell polarity, regulation of the cytoskeleton, signal transduction or other areas that complement existing strengths in our department and in any system (plant, animal, microbial). The central criteria for this position are excellence in research and the ability to teach undergraduate and graduate students with a high level of effectiveness. For information about the Department, visit our website: **http://sitemason.vanderbilt.edu/biosci.**

Applicants should send a letter of application together with a curriculum vitae, a statement of current and future research interests, three letters of recommendation, teaching evaluations, if available, and selected reprints to: **Cell Biology Search Committee, Department of Biological Sciences, Vanderbilt University, VU Station B 351634, Nashville, TN 37235-1634 U.S.A.** Review of applicants will begin **October 1, 2004**, and will continue until the position has been filled.

Vanderbilt University is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

Lillian Nelson Pratt Endowed Chair

Southwestern University
AT GEORGETOWN, TEXAS

The Department of Biology at Southwestern University invites applications from broadly trained **Evolutionary Biologists** for the Lillian Nelson Pratt Endowed Chair in Biology. Preference will be given to applicants with expertise in developmental and/or molecular approaches. Appointment will be at a rank commensurate with the experience of the individual filling the position, to begin August 2005. A PhD in a relevant discipline, a strong commitment to undergraduate teaching, and a record of distinction in both teaching and research are required.

Teaching responsibilities will include upper-level Evolutionary Biology for majors, participation in the Introductory Biology sequence, and possible additional courses as required by Departmental needs. The successful candidate may elect to participate in Southwestern's interdisciplinary Environmental Studies Program. The successful candidate will be expected to maintain a research program that actively involves undergraduates.

Southwestern University is a selective, undergraduate institution committed to a broad-based liberal arts, sciences, and fine arts education. Southwestern currently enrolls approximately 1,250 students and maintains a student to faculty ratio of 10 to 1. The University's endowment ranks among the highest per student of undergraduate institutions in the country. In addition to a number of other national organizations, Southwestern University is a member of two consortia of liberal arts colleges, the Associated Colleges of the South and the Annapolis Group. Located in Georgetown, Texas, 28 miles north of downtown Austin, Southwestern is affiliated with The United Methodist Church. Southwestern University is committed to fostering a diverse educational environment and encourages applications from members of groups traditionally under-represented in academia. For information concerning the University, visit our web site at **www.southwestern.edu.**

Interested persons should send a letter of interest, curriculum vitae, statements of teaching and research philosophies, graduate and undergraduate transcripts (unofficial), and three current letters of recommendation to: **Kendra Clovis, Faculty Secretary - Biology Search, Southwestern University, P.O. Box 770, Georgetown, TX, 78627-0770.**

Applications received by **October 22, 2004** will receive full consideration. For more information, contact the **Biology Department Chair, Dr. Rebecca Sheller, shellerr@southwestern.edu.**

Southwestern University is an Equal Opportunity Employer. EOE/M/F

PENNSTATE Department of **Chemistry**

PENN STATE UNIVERSITY, CHEMISTRY DEPARTMENT, FACULTY POSITIONS

Two Junior and two Senior level faculty positions are available for Fall 2005. All areas of chemistry will be seriously considered. The Chemistry Department at Penn State has recently moved into a new state-of-the-art building. Departmental research spans both traditional and non-traditional cutting-edge areas, and faculty members have opportunities to participate in university-wide life sciences, materials, environmental, and computational institutes. Appointees are expected to establish an exceptionally strong and highly visible research program that incorporates excellence in undergraduate and graduate education. Senior appointments should have a previous record of national and international distinction. Applicants should submit a curriculum vitae, a list of publications, and research plans to: Chair of the Search Committee, Box C, Department of Chemistry, 104 Chemistry Research Building, Pennsylvania State University, University Park, PA 16802. Junior applicants should also arrange to have three letters of recommendation sent to this address. Review of applications will begin on October 1, 2004 and continue until the positions are filled. For more information and an application form: http://www.chem.psu.edu/facultyapplication.html. Penn State is committed to affirmative action, equal opportunity and the diversity of its workforce.

National Tsing Hua University
College of Nuclear Science
Hsinchu, Taiwan, ROC

The College of Nuclear Science of the National Tsing Hua University (NTHU) in Hsinchu, Taiwan has faculty openings at all levels to begin August 1, 2005. We are seeking outstanding candidates in the following fields:

For the Department of Engineering and System Science:

1. Energy Engineering and System: Hydrogen Technology, Fuel Cell, Energy System, Advanced Nuclear Reactors, Radiation Biomedical application.
2. Plasma Science and Engineering: Plasma Chemistry, Plasma Light source, Plasma Application.
3. Nano-and Micro-Electro-Mechanical System: Nano Measurement and Analysis, Nano and Micro Biomedical Engineering, Micro photoelectrical Processing and Circuit Design for Biomedical System.

For the Department of Nuclear Science:

1. Molecular biophotonics: Gene Chip and Biomedical Application (with Biomedical Background), Nano Biomedicine (Single Molecular Manipulation), Molecular Imaging (Radiopharmapseutical and Therapy).
2. Environmental Molecular Science: Nano/Ultra Trace Analysis, Contaminant Migration and Environmental Biological Effect.
3. Medical Physics: Radiation Therapy, Radiation diagnostics and Imaging, Nuclear Medicine, and Health Physics.

Cross-disciplinary appointments with other colleges in the University are possible and encouraged. Excellence in research and teaching are the main qualifications for consideration to an appointment. Proficiency in Chinese or English is a requirement as NTHU intends to become a fully bilingual institution within ten years.

The applicant must indicate the specific department that he or she is applying for, and provide the personal resume, a description of current academic research and future plans, and any other helpful information. Please send all the materials to

College of Nuclear Science
National Tsing-Hua University,
101, Sec.2, Kuang Fu Road Hsinchu 30013, Taiwan, R.O.C.

no later than October 1, 2004. Or else send it in before February 1, 2005 for the second round.

After passing the primary review, the candidates will be asked to provide three recommendation letters (one of which has to come from the thesis advisor if they are applying for assistant professor) each. Should you have any question please reach us by the email: nuclear@my.nthu.edu.tw.
Our internet site: http://www.ess.nthu.edu.tw/%7Ecollege.

MAYO CLINIC

Translational Immunovirology and Biodefense Faculty Position

Rochester, Minnesota

The Department of Medicine at Mayo Clinic in Rochester, MN invites applications from persons interested in conducting laboratory-based research in the fields of Translational Immunovirology and Biodefense. Successful applicants will receive substantial intramural support and will have an established extramurally funded research program that would support cross-disciplinary research programs within the Department of Medicine. Position responsibilities include securing further extramurally funded support for research, supporting the Department's Translational Immunovirology and Biodefense Center of Excellence and interaction with Departmental divisions, other Departmental programs or other Departments.

The successful candidate will have an MD, Ph.D. or an MD/Ph.D. degree(s) and must be eligible for hire at Mayo.

To learn more about Mayo Clinic and Rochester, MN, please visit **www.mayoclinic.org**

Interested applicants should submit a curriculum vitae, a statement of research interests and goals, along with the name of three references by October 15, 2004 to:

Gregory A. Poland, M.D.
Director, Program in Translational Immunovirology and Biodefense
611C Guggenheim Building
Mayo Clinic and Foundation
200 First Street, SW
Rochester, MN 55905

Mayo Foundation is an affirmative action and equal opportunity educator and employer. Post offer/pre-employment drug screening is required.

THE OHIO STATE UNIVERSITY

FACULTY POSITION IN BIOCHEMISTRY

The Ohio State University

The Department of Biochemistry at The Ohio State University invites applications for a **Tenure-Track Faculty Position**, preferably at the Assistant Professor level, as part of a multi-year effort involving several hires in our continuing efforts to develop excellence in structural biochemistry. Macromolecular structure/function, folding and assembly, and protein-protein and protein–nucleic acid interactions in the post-genomics/proteomics era are themes that are being developed to complement the current research interests of our faculty (http://www.biosci.ohio-state.edu/~biochem). All highly qualified candidates will receive consideration with some preference given to those with research interests in the study of membrane protein systems, protein-protein and/or other biomolecular interactions and whose research utilizes current molecular biological, proteomic, and/or physical biochemical approaches that complement the existing faculty.

The candidate should have a Ph.D. degree or its equivalent with a strong background in biochemistry, at least two years of postdoctoral experience, and a strong record of accomplishment. A commitment towards developing an independent and creative research program supported with extramural funds and to excellence in teaching at both the graduate and undergraduate levels is essential.

Please send curriculum vitae, a summary of research accomplishments, and a three-page description of future research plans to the **Faculty Search Committee, Department of Biochemistry, The Ohio State University, 484 West 12th Avenue, Columbus, OH 43210.** Candidates should also arrange for three letters of recommendation to be sent to the department. Review of applications will begin October 1, 2004 and continue until the position is filled.

OSU is an Equal Opportunity/Access and Affirmative Action Employer

Yale University
Faculty Positions in Ecology and Evolutionary Biology

The Department of Ecology and Evolutionary Biology at Yale University invites applications for several faculty positions at either the senior or junior level. We have a special interest in the following fields:

(1) theory, both evolutionary and ecological, including computational approaches;
(2) phylogenetic and other historical approaches to ecological questions;
(3) comparative biology that involves intimate acquaintance with organisms and active use of the Peabody Museum collections;
(4) interactions, including symbioses, mutualisms, and host-pathogen interactions.

A record of outstanding achievement and a promising research program are more important than the specific research area. Interested candidates should submit their CVs, three relevant reprints or manuscripts, a brief research and teaching statement, and the names and addresses of four potential evaluators **by 30 September 2004**. Send materials to: **Department of Ecology and Evolutionary Biology, Yale University, P.O. Box 208106, New Haven, CT 06520-8106 USA attn: Francine Horowitz.** The Department is described at **www.eeb.yale.edu**.

Yale University is an Equal Opportunity/ Affirmative Action Employer. Men and women of diverse racial/ethnic backgrounds and cultures are encouraged to apply.

FACULTY POSITIONS (2) IN NEUROSCIENCE

The Department of Neurobiology of the Northeastern Ohio Universities College of Medicine (NEOUCOM) **(website: http://www.neoucom.edu)** seeks applications for two (2) tenure-track positions with a proposed starting date of July 1, 2005. One position is at the Assistant Professor level and the other at the Assistant or Associate Professor level. Successful candidates at the Assistant Professor level will establish an active externally-funded research program, so applicants must demonstrate research productivity and the capability of attracting external funding. Candidates at the Associate Professor level should have extramural research support at the date of hire. Candidates must have an earned Ph.D. and/or M.D. and have at least 2 years of postdoctoral research experience. Research in the department focuses on sensory systems, including molecular, cellular and systems-level processing, plasticity, neurochemical anatomy, and modulation by other systems. Individuals working in areas that strengthen or complement ongoing research are particularly encouraged to apply.

The successful candidates will teach in the Medical Neuroscience course and in graduate courses, participate in an interdisciplinary graduate program, and develop graduate courses in their field of expertise. Previous educational and teaching background in neuroscience is a plus. Females and underrepresented minorities are especially encouraged to submit an application.

NEOUCOM participates in a consortium with Kent State University, University of Akron, Youngstown State University and eight teaching hospitals to offer combined B.S./M.D. Degrees. Basic medical science faculty participate in Ph.D. graduate programs in conjunction with the School of Biomedical Sciences at Kent State University. Graduate training opportunities in Biomedical Engineering are available in collaboration with the Institute for Biomedical Engineering Research at The University of Akron.

Applications must include a curriculum vita, a letter of personal statement describing research interests, goals and plans for securing external support, teaching philosophy & experience, as well as the names and complete addresses of three references. Applications are requested by October 15, 2004, but will be accepted until the positions are filled. Send materials to: **Human Resources, c/o Raymond E. Papka, Ph.D., Professor and Chair, Department of Neurobiology, Northeastern Ohio Universities College of Medicine, PO Box 95, Rootstown, OH 44272.** Electronic files, attention: Neurobiology search, may be sent as attachments or as pdf files to: **jobs@neoucom.edu**

NEOUCOM
NORTHEASTERN OHIO UNIVERSITIES
COLLEGE OF MEDICINE

NEOUCOM is an Equal Opportunity Employer and Educator

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

Faculty Positions in Chemical Engineering

at the Swiss Federal Institute of Technology Lausanne (EPFL)

The EPFL invites applications for positions of Professor (tenure track assistant professor, associate professor or full professor) in its Institute of Chemical Sciences and Engineering (ISIC).

We seek outstanding scientists with recognized accomplishments in any field of chemical engineering oriented toward the experimental or theoretical biomolecular and bioprocess sciences.

The successful candidate will establish and lead a vigorous, independent research program, interact with existing projects and be committed to excellence in teaching at both the undergraduate and graduate levels. Significant start-up resources and research infrastructure will be available.

Applications with curriculum vitae, publication list, concise statement of research and teaching interests as well as the names and addresses (including email) of at least five references should be sent by **October 15, 2004,** to:

Professor Thomas Rizzo
Head of the search committee
Institute of Chemical Sciences and Engineering
Faculty of Basic Sciences
EPFL
CH-1015 Lausanne, Switzerland

For additional information, please consult: http://www.epfl.ch, http://sb.epfl.ch and http://isic.epfl.ch

The EPFL is an equal opportunity employer.

FOUR POSITIONS IN GENETICS/GENOMICS/MOLECULAR BIOLOGY

The University of Texas at Arlington

The Department of Biology at The University of Texas at Arlington invites applications for four tenure-track positions at the rank of Assistant Professor. Exceptional candidates at other ranks will be considered. We seek eukaryotic and prokaryotic genomicists to contribute to the department's focus in genetics and genomics. Additional hires will add to this core group or complement it. We are interested in individuals using prokaryotic or eukaryotic systems to address questions in population, evolutionary or ecological genetics/genomics; quantitative or developmental genetics; molecular evolution and related areas. Applicants must have a Ph.D. and a demonstrated record of research productivity commensurate with their experience. The successful candidates will be expected to establish vigorous, extramurally funded research programs and participate in both graduate and undergraduate education. The Department offers several degrees including a Ph.D. in quantitative biology. Located in the Dallas/Fort Worth metropolitan area, UTA is a fast-growing, comprehensive university that is the second largest in the University of Texas system. Hiring will be contingent on the completion of a satisfactory criminal background investigation for security sensitive positions. Additional information is available at the website: **http//www.uta.edu/biology/**.

Applicants should submit curriculum vitae; copies of up to five significant publications; statements of research and teaching interests and philosophy; and the names, e-mail address, and telephone numbers of four persons who can provide letters of reference. Review of completed applications will begin **October 15, 2004**, and will continue until the positions are filled. Send applications to: **Genetics Search Committee, Department of Biology, University of Texas at Arlington, Box 19498, 501 South Nedderman Drive, Arlington TX 76019-0498**.

UTA is an Equal Opportunity/Affirmative Action Employer.

FACULTY POSITIONS
MARINE BIOLOGY AND VERTEBRATE PHYSIOLOGY

The Department of Biology at Occidental College invites applications for two **tenure track faculty positions**, one in **Vertebrate Physiology**, using cellular and/or molecular approaches, and one in **Marine Biology**. Rank and salary are subject to qualifications; hires at a senior level will be considered. Applicants should have a strong commitment to educating undergraduates through teaching and research. For both positions the successful candidate is expected to develop a rigorous research program involving undergraduates. Both faculty members are expected to participate in teaching introductory and intermediate level biology courses and to develop an upper level course in their area of specialty. Many opportunities exist for faculty to participate in interdisciplinary programs such as Biochemistry, Cognitive Science, the Core Program, Psychobiology, or Women's Studies. Faculty are expected to participate in the College Core program, either by teaching introductory science classes or teaching interdisciplinary core classes. Occidental is a nationally ranked small liberal arts college with excellent research and teaching facilities, located in Los Angeles, near Caltech and other research institutions. The College's location allows for outstanding opportunities for access to marine research facilities. Occidental is nationally recognized for its broadly diverse student body, and for its outstanding undergraduate research program. For more information on Occidental College, please visit our web site at **www.oxy.edu**.

Applicants should submit a letter of interest demonstrating a commitment to academic excellence in a diverse liberal arts environment, curriculum vitae, separate statements of research and teaching interests, copies of significant publications, and have three letters of reference sent to: **Faculty Search Office M8888**; addressed either: **Attention: Roberta Pollock, Vertebrate Physiologist Search Chair or Attention: Elizabeth Braker, Marine Biologist Search Chair; Occidental College; 1600 Campus Road; Los Angeles, CA 90041.** Review will begin September 30, 2004, and continue until the positions are filled.

Occidental College is an equal opportunity employer. The College is committed to academic excellence in a diverse community and supporting interdisciplinary and multicultural academic programs that provide a gifted and diverse group of students with an educational experience that prepares them for leadership in a pluralistic world. Women and minorities are strongly encouraged to apply.

UNIVERSITY OF PENNSYLVANIA
SCHOOL OF DENTAL MEDICINE

TENURE-TRACK POSITION IN BIOCHEMISTRY

The Biochemistry Department at the University of Pennsylvania School of Dental Medicine seeks a tenure-track Assistant or Associate Professor with research interests in any area of biochemistry or molecular cell biology that complements the existing strengths of the institution. Our Department (**http://biochem.dental.upenn.edu/biochem/**) is part of a vibrant research community within the School of Dental Medicine with research strengths in skeletal biology, infectious diseases and wound healing, and has strong interactions with nearby colleagues at the Schools of Medicine, Veterinary Medicine and Engineering. Requirements include a strong record of research accomplishment, a Ph.D. in Biochemistry or Molecular Biology, and at least two years of postdoctoral experience. The successful applicant must demonstrate his/her potential for establishing an externally funded research program and must have strong teaching skills. Applications are particularly invited from individuals who also have clinical degrees (D.M.D., M.D. or D.O.).

Applicants should send a curriculum vitae, statement of research interests and a list of three referees to:

Dr. Sherrill L. Adams
Professor and Chair of Biochemistry
University of Pennsylvania
School of Dental Medicine
240 S. 40th Street
Philadelphia, PA 19104-6030

E-mail applications in the form of Microsoft Word, WordPerfect or Adobe Acrobat (PDF) files can be sent to: **sherri@biochem.dental.upenn.edu.** Applications will be reviewed beginning **November 1, 2004**.

The University of Pennsylvania is an Equal Opportunity Employer. Minorities, females, individuals with disabilities, and veterans are encouraged to apply.

TENURE-TRACK FACULTY POSITION
Assistant Professor – Molecular Virology

The Department of Molecular Microbiology and Immunology (MMI) **http://www.missouri.edu/~mmiwww** at the University of Missouri-Columbia, School of Medicine, in Columbia, MO, invites applications for a **new tenure-track Assistant Professor level position in virology.** Preference will be given to individuals using contemporary approaches to address important aspects of viral pathogenesis, virus-cell interactions, viral transduction biology, and/or virus-based gene therapy. Applicants grounded in basic mechanisms of molecular and cellular biology are strongly encouraged. Applicants must possess the Ph.D., M.D., or equivalent degree, and have appropriate post-doctoral training. Successful candidates will be expected to establish an outstanding, independent research program that will attract continued extramural funding, and participate in the teaching and training missions of the Department. Laboratory space will be located in the new MU Life Sciences Center (LSC) (**http://lifesciences.missouri.edu/**), a state-of-the-art, multi-disciplinary research and teaching facility, opened in August, 2004, which provides a highly interactive scientific environment. It will eventually house some 35 investigators (approximately half being new hires), and will serve as the hub of Life Sciences research on the MU-Columbia campus. Proteomics, imaging, and DNA core facilities, as well as a BL3 laboratory, are housed in the building, and core facilities for flow cytometry, electron microscopy, structural biology, mouse transgenics, ES cell manipulations, and hybridoma production, are in close proximity (**http://biotech.missouri.edu**). Salary and start-up packages are highly competitive.

Interested candidates should submit a curriculum vitae, a statement of research interests and future research goals, and contact information for at least three referees to the address below (e-submission preferred). Applications will be reviewed starting September 15, 2004, and until the position is filled. **Molecular Virology Search Committee, Attn: Ms. Shelly Crawford, Office Supervisor, M616 Medical Sciences Building, Dept. of Molecular Microbiology and Immunology, University of Missouri-Columbia, School of Medicine, Columbia, MO 65211; (573) 882-8989; crawfords@health.missouri.edu.**

The University of Missouri is an AA/EOE. To request ADA accommodations, please contact (573) 884-7278 (V/TTY). Women and minorities underrepresented in biomedical research are encouraged to apply.

FACULTY POSITIONS

The Biological Sciences Department within the College of Science and Mathematics at California Polytechnic State University is accepting applications for two full-time, academic year, tenure track positions at the assistant professor rank beginning September 2005 as listed below.

Animal Physiologist (Requisition #100385). Primary teaching responsibilities will include human anatomy & physiology and general physiology. Other teaching responsibilities may include introductory biology, a graduate level course in organismal biology, and other undergraduate and graduate courses as appropriate to background and training. The position is open to all specialties including, but not limited to, neurophysiology (including sense receptors), endocrine/reproductive physiology, and comparative physiology. Use of invertebrate or lower vertebrate research systems is desirable but not required.

Medical Microbiologist (Requisition #100386). Primary teaching responsibilities will include medical microbiology, introductory microbiology, immunology, and other undergraduate and graduate courses as appropriate to background and training. Also desirable are a strong background in immunology and epidemiology and postdoctoral or equivalent experience.

The successful candidate must have a strong commitment to undergraduate teaching, curriculum development, and implementation of a student-centered research program. Ph.D. in related field required at time of hiring. Salary is commensurate with qualifications and experience.

To apply, visit **WWW.CALPOLYJOBS.ORG**, complete an online application, and submit it to **Requisition #100385 (Animal Physiologist)** or **Requisition #100386 (Medical Microbiologist)**. Mail curriculum vitae, a statement of teaching philosophy, a statement of professional goals, and arrange to have official graduate transcripts and three letters of recommendation sent to: **Dr. V. L. Holland, Chair, Biological Sciences Department, California Polytechnic State University, San Luis Obispo, CA 93407**. Review of applications will begin **November 1, 2004**. Applicants are strongly encouraged to have all materials submitted by **November 1**; applications received after this date may be considered. For questions, contact the Biological Sciences Department at **(805) 756-5241**.

Cal Poly is strongly committed to achieving excellence through cultural diversity. The university actively encourages applications and nominations of all qualified individuals. EEO.

TENURE-TRACK ASSISTANT PROFESSOR
Department of Neurobiology
David Geffen School of Medicine at UCLA

The Department of Neurobiology in the David Geffen School of Medicine at UCLA invites applications for a tenure-track faculty position at the Assistant Professor level. We seek outstanding candidates who will establish and maintain a vigorous, creative and independent research program and participate in collaborative projects within and outside the Department. We are particularly interested in system neuroscientists, especially those using non-human primates as research subjects, and/or using quantitative/computational approaches to understand fundamental neurobiological processes. Exceptional candidates in other areas of neuroscience are also encouraged to apply.

Applicants should have a PhD, MD, or equivalent, and postdoctoral training experience in neuroscience. The position includes a competitive start-up package and a salary commensurate with rank and experience. The appointment can start as early as July 1, 2005.

To apply, please send a curriculum vitae, a brief statement of current and future research plans, up to 5 reprints and the names of 3-5 references to:

Chair, Search Committee
Department of Neurobiology
David Geffen School of Medicine, UCLA
Box 951763
Los Angeles, CA 90095-1763

To receive full consideration, applications should be received by **December 1, 2004**.

UCLA is an Equal Opportunity/Affirmative Action Employer.

SYRACUSE UNIVERSITY
Department of Biology
Tenure-track Faculty Position in Biocomplexity

The Department of Biology at Syracuse University invites applications for a tenure-track position (Assistant to Full Professor) to be filled by August 2005. The successful candidate will have, or will develop, a strong, extramurally funded and highly innovative research program in ecology to join an emerging interdisciplinary research group in biocomplexity. The successful candidate will be one who uses terrestrial or aquatic systems to investigate questions related to plant ecophysiology, plant ecology, microbial ecology, trophic interactions, or ecosystem dynamics. Successful applicants will complement current research strengths within the department and university related to functioning of complex biological systems in different environments. The Department and the University place a high priority on effective teaching. Successful candidates will be expected to teach at undergraduate and graduate levels.

Successful candidates will join a highly productive faculty with strong links to other programs at Syracuse University, including engineering, environmental policy, biochemistry and earth sciences. The Department is in the midst of an exciting growth period, having hired seven new faculty in the past four years. We anticipate hiring six-ten more new faculty over the next five years. Specific information about individual Biology faculty research programs may be found on our website: **http://biology.syr.edu/facultyresearch/facultyresearch.html**

The Syracuse biocomplexity group also has close intellectual ties to more than 60 other faculty at several other universities including the nearby State University of New York Environmental Science and Forestry school (SUNY-ESF) and Cornell University. Collaborations among the faculty in this group would allow successful applicants to explore several new interdisciplinary funding initiatives at NSF, including NSF's Biocomplexity Initiative, Emerging Frontiers, and Biology & Mathematics programs.

Applicants should forward a curriculum vitae, a description of past research accomplishments, a clearly focused description of his/her proposed future research goals and a statement of teaching interests. We also request that applicants have at least three letters of reference sent. Please include the name, address, phone number and e-mail address of each of your references. We invite applicants to submit materials electronically as a single PDF file to: biosearch@cas.syr.edu. The position will be open until filled, but to be assured your application receives full consideration, we urge that you arrange to have all necessary materials to us by October 15, 2004.

Applications and reference letters should be addressed to: **Larry Wolf, Chair, Biocomplexity Faculty Search, Department of Biology, 130 College Place, Syracuse University, Syracuse, NY 13244**

Syracuse University is an affirmative action/equal opportunity employer with a strong commitment to equality of opportunity and a diverse workforce.

FACULTY POSITIONS IN CELL AND MOLECULAR BIOLOGY

The Department of Cell and Molecular Biology at Tulane University (**http://cell.tulane.edu/**) anticipates filling two tenure-track positions beginning July 1, 2005, at the level of Assistant Professor. Targeted are individuals whose research interests focus in either Developmental Biology and/or Neuroscience. The department has targeted Neuroscience and Developmental Biology as areas for future growth. Applicants must have a Ph.D., at least 2 years of postdoctoral experience, a strong publication record, and show potential for obtaining external funding. The successful applicant will be expected to establish a vigorous, independent research program and to participate in graduate and undergraduate teaching. Opportunities exist for research collaborations and participation in the Tulane Cancer Center, the Tulane Primate Center, the Tulane/Xavier Center for Bioenvironmental Research, the Tulane Neuroscience Program, and the Interdisciplinary Graduate Program in Molecular and Cellular Biology.

Applicants should send curriculum vitae, a brief statement of research interests and three letters of recommendation by **November 15, 2004** to:

Dr. Ken Muneoka, Chair
Department of Cell and Molecular Biology
Tulane University
New Orleans, LA 70118

Tulane University is an Equal Opportunity/ Affirmative Action Employer and encourages minority and female applicants to apply.

Temple University Engineering

Temple University's College of Engineering, located in the metropolitan area of Philadelphia, Pennsylvania, is searching for outstanding individuals to join its faculty. The College is planning an unprecedented period of growth characterized by focused recruitment of research-active faculty in an effort to increase its size by 25%. Interested individuals are urged to apply for the following openings:

Chair, Department of Electrical and Computer Engineering.
The new chair will have the rare opportunity to double the size of the department over the next few years. The department is strengthening its graduate and undergraduate program in computer engineering. Other areas of interest include Digital Logic Synthesis, Microelectronics, VLSI, and Bioengineering.

Faculty, Department of Electrical and Computer Engineering.
Applicants at all stages of their career, with interests in one or more of the department's areas of interest, are invited to apply.

Faculty, Mechanical (Bio-) Engineering.
The ideal candidate will have an interest in Bio-/Cellular Mechanics, Bio-MEMS, Nanotechnology, or Design, with a Ph.D. in Mechanical, Materials, or Bio-Engineering.

Faculty, Environmental Engineering.
Applicants should have a doctoral degree in Civil Engineering, Environmental Engineering, or a closely related field, and demonstrated research accomplishments preferably in Biological Treatment Processes, or in a field that complements the current departmental research strengths in Air Quality, Chemical Treatment Processes, Environmental Fluid Dynamics, and Contaminant Transport in rivers, soils and aquifers, and Hydrologic Processes.

Successful candidates will have, or be able to develop, significant research programs, and will provide effective instruction at undergraduate and graduate levels. Appointments are possible at all academic levels. Opportunities exist for collaboration with the School of Medicine, and the College of Science and Technology. Joint courtesy appointments are available. Salary and benefits for faculty are highly competitive and resources have been allocated for start-up.

Applicants should submit a curriculum vitae, a statement of research interests and plans, a brief description of teaching philosophy, and the names and addresses of four references. Please send all application materials to: **Search Committee, College of Engineering, Temple University, Room 330, 1947 North 12th Street, Philadelphia, PA 19122, or electronically to GRBaran@temple.edu.**

Equal Opportunity/Affirmative Action Employer.
Applications from women and minorities are encouraged.

FACULTY OF MEDICINE
GREAT MINDS FOR A GREAT FUTURE
University of Toronto

Department of Laboratory Medicine and Pathobiology

Academic Microbiology Position

The Department of Laboratory Medicine and Pathobiology, Faculty of Medicine, University of Toronto (**http://www.utoronto.ca/LabMedPathobiology**) is seeking applicants for one full-time faculty position either non-tenure or tenure-stream at the rank of Assistant Professor available July 1, 2005. We are particularly interested in individuals working in the areas of molecular and biochemical mechanisms of microbial disease, including virology. Candidates must have an MD or a PhD degree or equivalent, have completed significant postdoctoral training, and have an established track record of high quality research. Exceptional candidates with established funded research programs and a rank of Associate or Full Professor may be considered as well. Teaching experience at the undergraduate and graduate level is an important asset.

The successful candidate is expected to participate actively in graduate and undergraduate teaching programs, maintain a well-funded, independent research program and interact with other investigators at the University campus and the major affiliated teaching hospitals.

Applicants should submit curriculum vitae, description of their research accomplishments and the focus of their planned research program and the names of three referees by **15th November, 2004** or until the position is filled, to the **Chair, Academic Search Committee, Department of Laboratory Medicine and Pathobiology, Faculty of Medicine, University of Toronto, Room 110, 100 College Street, Toronto, Ontario, Canada, M5G 1L5**.

The University of Toronto is strongly committed to diversity within its community and especially welcomes applications from visible minority group members, women, Aboriginal persons, persons with disabilities, members of sexual minority groups, and others who may contribute to the further diversification of ideas.

All qualified candidates are encouraged to apply; however, Canadians and permanent residents will be given priority.

Institutes of Biomedical Sciences
Fudan University
RECRUITMENT

The Institutes of Biomedical Sciences, is a new research institute of Fudan University. The Institutes strive to contribute to the progress of biomedical research by studying basic mechanisms of human diseases, and to find new approaches to diagnostics and therapy. Five research institutes and four research centers, including Institute of Genomics, Institute of Proteomics and Systems Biology, Institute of Developmental Biology, Institute of Stem Cell and Tissue Engineering, Institute of Structural Biology and Pharmacy, Research Center of Cancer, Research Center of Cardio-Cerebral Vascular Disease, Research Center of Infectious Disease and Public Health, and Research Center of Pathology will be set up. **Positions of 9 Institute Directors, 60 Principal Investigators and Senior Research Scientists in the above nine research areas are open for application.** For more details, please visit the following website:

http://www.biomed.fudan.edu.cn

Interested individuals must send electronically a full CV (either English or Chinese) that includes which institute/center and position you applied for, history of training, employment, awards and achievements, a description within 3,000 words of intent and vision for the applied position. Please mail copies of five representative articles and three letters of recommendation for the Director position and the Principal Investigator and Senior Research Scientist positions to:

Miss Yan Jiang, Miss Tracy Wu
130 Dong An Road,
Institutes of Biomedical Sciences,
Fudan University, P.O.Box 281, Shanghai, 200032

Tel: 0086-21-5423 7307, 5423 7325
Fax: 0086-21-5423 7307
E-mail: biomed_nl@fudan.edu.cn

TENURE-TRACK FACULTY POSITIONS
Assistant Professors – Immunology

The Department of Molecular Microbiology and Immunology (MMI) (**http://www.missouri.edu/~mmiwww)** and the Department of Otolaryngology (**http://www.missouri.edu/~otohnswww**) at the University of Missouri-Columbia, School of Medicine, in Columbia, MO, invite applications for **two new tenure-track positions at the Assistant Professor level in the area of immunology**. Appointees will be expected to complement the current interdisciplinary immunology expertise in innate and adaptive immunity and to contribute to the developing research focus in the area of inflammation. Preference will be given to interactive individuals using modern molecular approaches to address problems in allergy, host responses to infection, and mucosal immunity in the upper respiratory tract. Applicants must have a PhD., MD., or equivalent degree, appropriate postdoctoral training and a demonstrated commitment to academic excellence. Successful candidates will be expected to establish and maintain outstanding, independent research programs that will attract external funding and to participate in the teaching and training missions of the Departments. Laboratory facilities on the 6th floor of the Medical School are modern and support facilities include state of the art core facilities. More information on the core facilities can be viewed at **www.biotech.missouri.edu**. Salary and start-up packages are commensurate with experience.

Interested candidates should submit to the address below (e-submission preferred) a curriculum vitae, a summary of current research interests and future research plans, and the names of at least three individuals for reference including their postal and email addresses and phone numbers. Applicants will be reviewed beginning September 15, 2004 and will be continued until the positions are filled. **Immunology Search Committee, Attn: Ms. Shelly Crawford, Office Supervisor, M616 Medical Sciences Building, Dept. of Molecular Microbiology and Immunology, University of Missouri-Columbia, School of Medicine, Columbia, MO 65211; (573) 882-8989; crawfords@health.missouri.edu**.

The University of Missouri is an AA/EOE. To request ADA accommodations, please contact (573) 884-7278 (V/TTY). Women and minorities under-represented in biomedical research are encouraged to apply.

Assistant Professor of Pharmacology

The Oregon State University Department of Pharmaceutical Sciences seeks an Assistant Professor in Pharmacology (tenure track) to begin work July 1, 2005. Candidates should possess a strong background in the creation, use, and analysis of genetically modified animals, preferably mice. A Ph.D. in pharmacology, biochemistry, molecular biology or a related field required as is a record of distinguished post-doctoral research.

For full consideration, send personal letter describing research/teaching interests, a curriculum vitae, and have three letters of reference submitted by **November 5, 2004**, to:

Mark Leid, Ph.D.
Chair, Pharmacology Search Committee
OSU Department of Pharmaceutical Sciences
203 Pharmacy Building
Corvallis, OR 97331-3507

TEL: 541-737-5809
FAX: 541/737-3999
Internet: Mark.Leid@oregonstate.edu

A complete job description can be found at:
http://www.oregonstate.edu/jobs/

OSU is an AA/EOE.

ASSISTANT PROFESSOR
CARDIOVASCULAR BIOLOGY
DEPARTMENT OF PHARMACOLOGY
UNIVERSITY OF WASHINGTON

Applications are invited for a tenure-track faculty position at the **ASSISTANT PROFESSOR** level in the Department of Pharmacology with a focus in cardiovascular biology. A PhD or MD degree and postdoctoral research experience are required; candidates with MD/PhD training are especially encouraged to apply. Selection will be based on scientific excellence and the potential to establish an outstanding independent research program using molecular, cellular, or physiological approaches to research problems relating to the cardiovascular system. The successful candidate will teach in graduate and medical courses, participate in graduate student training, and engage in patient care in medicine or cardiology if appropriate. Information about the department and its current research interests can be obtained at **http://depts.washington.edu/phcol/**. The committee will begin to review applications beginning **November 1, 2004** and will accept inquiries until the position is filled. The anticipated start date of the successful candidate will be July 1, 2005. Applicants should send their curriculum vitae, statement of research plans, and three letters of recommendation to: **Neil M. Nathanson, Ph.D., Chair, Cardiovascular Biology Search Committee, Department of Pharmacology, Box 357750, University of Washington, Seattle, WA 98195-7750**.

The University of Washington is an Affirmative Action, Equal Opportunity Employer. The University is building a culturally diverse faculty and staff and strongly encourages applications from women, minorities, individuals with disabilities and covered veterans.

SYRACUSE UNIVERSITY
DEPARTMENT OF BIOLOGY
Tenure-track Faculty Position in Cell Signaling/Cell Regulation

The Department of Biology at Syracuse University invites applications for a tenure-track position (Assistant to Full Professor) to be filled by August 2005. The successful candidate will have, or will develop, a strong, extramurally-funded research program which addresses cell signaling/cell regulation issues utilizing animal, plant or microbial models. We particularly seek an individual using a biochemical and/or a genetic approach to address cell signaling/regulation questions. The Department and the University place a high priority on teaching. The successful candidate will be expected to teach effectively at the undergraduate and graduate levels.

The Department of Biology is in the midst of an exciting growth period, having hired seven new faculty in the past four years. We expect to hire 6-10 more new faculty over the next five years. Additionally, the Biology, Chemistry and Physics Departments at Syracuse University are undertaking a joint initiative to develop a strong interactive cell signaling/regulation group possessing the breadth of experimental approaches and expertise necessary for research success. Information about this interdepartmental initiative can be found at: http://cell-signaling.syr.edu. Ample opportunities for research collaboration exist within Syracuse University as well as at the State University of New York-Upstate Medical University, located just two blocks from the Syracuse University Biology Department and the State University of New York Environmental Science & Forestry, located immediately adjacent to the Syracuse University campus. Specific information about our department and current Biology faculty research programs are found on our website: **http://biology.syr.edu/facultyresearch/facultyresearch.html**

To apply, send a curriculum vita, a description of past research accomplishments, a clearly focused description of your future research goals and a statement of teaching interests. We also request that applicants have at least three letters of reference sent directly to the address below. Please include the name, address, phone number and e-mail address of each of your references. We invite applicants to submit their materials electronically as a single PDF file to: biosearch@cas.syr.edu and to urge their reference letter writers to likewise submit their letters electronically to the above address. The position will be open until filled, but to assure your application receives full consideration, all necessary materials should be submitted by October 15, 2004.

Applications and reference letters should be addressed to: **Gerda E. Breitwieser, Ph.D., Cell Signaling Faculty Search, Department of Biology, 108 College Place, Syracuse University, Syracuse, NY 13244**

Syracuse University is an affirmative action/equal opportunity employer with a strong commitment to equality of opportunity and a diverse workforce.

FACULTY POSITION
CELLULAR NEUROBIOLOGY

The Department of Biological Sciences and the John F. Kennedy Center For Research On Human Development at Vanderbilt University seek candidates for a tenure-track, assistant professor faculty position in cellular neurobiology. Targeted areas of interest include the cytoskeleton, membrane/protein trafficking, cell motility and/or cell adhesion. The central criteria for this position are excellence in research and the ability to teach undergraduate and graduate students with a high level of effectiveness. For information about Vanderbilt biological science and neuroscience faculty visit **http://sitemason.vanderbilt.edu/biosci**, **https://medschool.mc.vanderbilt.edu/facultydata**, **http://medschool1.mc.vanderbilt.edu/brain_institute/**. The successful candidate will be a member of the Vanderbilt Kennedy Center (**http://www.vanderbilt.edu/kennedy/**).

Applicants should send a letter of application together with curriculum vitae, a statement of current and future research interests, three letters of recommendation, and selected reprints to: **Cellular Neurobiology Search Committee, Department of Biological Sciences, Vanderbilt University, VU Station B 351634, Nashville, TN 37235-1634 U.S.A.** Review of applicants will begin **September 1, 2004**, and will continue until the position has been filled.

Vanderbilt University is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

Faculty Position
in Molecular/Cellular Neuroscience

Washington University in St. Louis

Department of Anatomy and Neurobiology

Two faculty positions at Washington University School of Medicine in St. Louis, MO are available for individuals taking innovative molecular or cellular approaches to fundamental questions relating to synaptic function or development. These positions are in the Department of Anatomy & Neurobiology (**http://pcg.wustl.edu/**) and will be at the Assistant Professor or Associate Professor level. The department houses 22 active research labs in neurobiology, and is part of a much larger inter-departmental neuroscience program (program website **http://neuroscience.wustl.edu/**). Excellent shared facilities are available for molecular and cellular neuroscience, including imaging (electron and optical microscopy), and mouse genetics (generation and behavioral analysis of transgenic and knockout lines). Both the department and the neuroscience program offer numerous opportunities for scientific interactions and collaborations.

To apply: Send by email attachment one PDF or Word file that includes your CV, research summary, and names and email addresses of three references. Send one file only, limited to 10 pages to **susan@brainvis.wustl.edu**. In addition, please arrange for three letters of recommendation to be sent to: **Dr. David Van Essen**, via email to **susan@brainvis.wustl.edu**. Applications and letters must be received by **December 1, 2004**.

AA/EOE M/F/D/V.

For *M. tuberculosis* Molecular Biologist

The Biodesign Institute, an emerging leader in biomedicine and biotechnology, and the School of Life Sciences, Arizona State University, invite applications for an Assistant Professor tenure-track position from individuals with strong motivation to understand the mechanisms of pathogenesis, including regulation of gene expression, intracellular physiology, and/or pathogen-host interactions, of *Mycobacterium tuberculosis*. Candidates must have a doctoral degree at the time of appointment and demonstrate potential in teaching and research in related discipline. At least two years of postdoctoral research experience in relevant discipline is desirable. The successful candidate is expected to develop an innovative, extramurally funded and independent research program, participate in undergraduate and graduate education in the School of Life Sciences, mentor undergraduates, graduates and postdoctoral fellows, and interact in the multidisciplinary consortium that comprises The Biodesign Institute. The successful candidate will receive a competitive start-up package and teaching load compatible with high research productivity.

To apply, send a cover letter, a curriculum vitae, three representative publications, statements of future research plans and teaching philosophy and interests, and arrange for three letters of reference to be sent. Letters of reference, but not application materials, may be sent by email. The closing date for receipt of applications is **30 September 2004**; if not filled, applications will be evaluated weekly thereafter until the search is closed. Anticipated start date is 16 August 2005. Applications and email inquiries should be sent to:

Josephine Clark Curtiss, Chair
Molecular Biology Search Committee
c/o Ms. Nancy Lesko
School of Life Sciences
PO Box 874501
Tempe, AZ 85287-4501
email: nclesko@asu.edu

ASU is an Affirmative Action/Equal Opportunity Employer.

Chair
Department of Pharmaceutical Sciences
School of Pharmacy
University of Pittsburgh

In the 215 years since its founding, the University of Pittsburgh has evolved into an internationally recognized center of learning and research that is known as one of the finest public institutions in the country. The School of Pharmacy is located on the University's Oakland campus in Pittsburgh, where sixteen schools, including the six schools of the health sciences, enjoy technologically advanced resources and extensive opportunities for collaborations on its urban campus. The School of Pharmacy is affiliated with the internationally renowned University of Pittsburgh Medical Center (UPMC), the region's largest and finest network of tertiary, specialty, and community hospitals. Collectively, these educational, research, and clinical facilities provide one of the nation's greatest, most complete centers for health sciences research, patient care, and teaching. The School of Pharmacy, which has been among the top ten schools based on NIH funding for the past four years, is home to the Center for Pharmacogenetics, the Center for Education and Drug Abuse Research, and the Pharmacodynamic Research Center, and enjoys a national reputation for the Clinical Pharmaceutical Scientist Program.

The school invites applications and nominations for the chair of its Department of Pharmaceutical Sciences. The Department of Pharmaceutical Sciences includes faculty researchers in gene therapy and drug delivery, pharmacokinetics/dynamics, medicinal and natural products chemistry, drug discovery, pharmacology, and both pharmacodynamic and molecular modeling.

The successful candidate must have a doctorate in the biomedical sciences or relevant discipline, and be a superb communicator and leader who will be able to take the department to the next level of excellence. An active research program is a requisite, as is a strong commitment to professional and graduate education. The ideal candidate will be appointed at the rank of professor with the expectation of tenure for this calendar-year appointment. Salary will be commensurate with qualifications and experience. Applications should consist of a letter of interest and curriculum vitae. In order to receive full consideration, applications should be received by **October 1, 2004**. Applications should be addressed to: **Randall B. Smith, PhD, Search Committee Chair, School of Pharmacy, University of Pittsburgh, 1104 Salk Hall, Pittsburgh, PA 15261.**

The University of Pittsburgh is an Affirmative Action, Equal Opportunity Employer

NORTHWESTERN UNIVERSITY

Neurobiologist
Tenure-track faculty position

The Department of Neurobiology and Physiology in the Weinberg College of Arts and Sciences seeks to recruit a neurobiologist at the Assistant Professor level. Applicants holding a Ph.D or M.D. degree, and demonstrating an outstanding record of scientific achievement will be considered. We are particularly interested in individuals whose research addresses fundamental issues in cellular neurobiology and who show potential for innovative scholarship and excellence in teaching. Successful candidates will be expected to pursue a high-profile research program attracting substantial extramural funding. The appointee will join Departmental colleagues in the new Pancoe/ENH Life Sciences Pavilion, with access to state-of-the-art facilities. He/she may also interact with colleagues in the Northwestern University Institute for Neuroscience, Center for Functional Genomics, Center for Reproductive Science, Center for Sleep and Circadian Rhythms, Dept. of Biochemistry, Molecular Biology, and Cell Biology and the Robert H. Lurie Cancer Center. Applicants should submit a curriculum vitae and description of research plans to: **Search Committee Chair, Department of Neurobiology and Physiology, Northwestern University, 2205 Tech. Dr., Evanston, IL 60208**. Applicants should also arrange to have three letters of recommendation sent to the same address. Applications received by **November 15, 2004** will be ensured full consideration.

AA/EOE. Women and minority candidates are encouraged to apply.

BSC BRIDGEWATER STATE COLLEGE

Assistant Professor
Cell Biology

The Department of Biological Sciences, Bridgewater State College, Bridgewater, MA, invites applications for a full-time tenure-track position beginning Fall 2005. The position requires teaching cell biology, introductory biology for both majors and non-majors, and upper level courses to augment the department's biomedical/molecular offerings.

The successful candidate must have an earned Ph.D. by May 2005 and excellent communication skills. A strong commitment to teaching and research in an undergraduate setting, as well as to advising students and supervising original undergraduate research are required. Participation in equipment procurement is required. Teaching experience is preferred as is post-doctoral research.

Please submit curriculum vitae, a letter describing teaching and research interests, official transcripts, and names, addresses and telephone numbers of three professional references to: **Office of Human Resources, Bridgewater State College, Bridgewater, MA 02325. Review of applications will continue until the position is filled.**

Bridgewater State College is an affirmative action/equal opportunity employer which actively seeks to increase the diversity of its workforce.

http://www.bridgew.edu

BSC BRIDGEWATER STATE COLLEGE

Assistant Professor
Organic Chemistry

The Department of Chemical Sciences, Bridgewater State College, Bridgewater, MA, invites applications for a new full-time, tenure track position beginning in August 2005.

The successful candidate will have a strong commitment to undergraduate teaching (especially organic chemistry and introductory chemistry) and to developing a research program appropriate to an undergraduate setting (for more information on undergraduate research at Bridgewater State College, see www.bridgew.edu/ATP/). A Ph.D. and post-doctoral experience in organic chemistry or a related area are required, as are excellent oral and written communication skills. Prior teaching experience is preferred.

For consideration, submit a statement describing your teaching philosophy and research plans, a curriculum vita and official transcripts to: **Office of Human Resources, Bridgewater State College, Bridgewater, MA 02325.** Also, arrange to have three letters of recommendation sent to the same address. Review of complete applications will begin October 12, 2004 and continue until the position is filled.

Bridgewater State College is an affirmative action/equal opportunity employer which actively seeks to increase the diversity of its workforce.

http://www.bridgew.edu

FACULTY POSITION
MOLECULAR GENETICS

The Department of Biological Sciences at Vanderbilt University seeks candidates to fill a tenure-track faculty position in molecular genetics. While all applications are welcome, we are especially interested in candidates studying replication, recombination, repair, protein or RNA targeting, cytoskeleton, or intracellular organization in any system (plant, animal, microbial). The central criteria for this position are excellence in research and the ability to teach undergraduate and graduate students with a high level of effectiveness. For information about the Department, visit our website: **http://sitemason.vanderbilt.edu/biosci**.

Applicants should send a letter of application together with curriculum vitae, a statement of current and future research interests, three letters of recommendation, teaching evaluations, if available, and selected reprints to: **Molecular Genetics Search Committee, Department of Biological Sciences, Vanderbilt University, VU Station B 351634, Nashville, TN 37235-1634 U.S.A.** Review of applicants will begin **October 1, 2004**, and will continue until the position has been filled.

Vanderbilt University is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are encouraged to apply.

NEUROBIOLOGY
FACULTY POSITIONS
UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE

The Department of Anatomy & Neurobiology is recruiting new tenured/tenure track faculty positions in Neuroscience. Appointments will be made at **ASSOCIATE** or **FULL PROFESSOR** ranks.

We have recently moved into new space and are especially seeking applications from candidates who will complement the Department's existing strengths in neural systems, cellular physiology, developmental neurobiology and neuroendocrinology. Of particular interest are candidates using innovative genetic, molecular biological, cellular, integrative or computational approaches to understand function or plasticity of the mammalian CNS.

Our facilities include state-of-the-art core laboratories in molecular neurobiology, imaging, neurophysiology and neuroanatomy. We offer an outstanding intellectual and collaborative environment with highly competitive salary and start-up packages. The department has NIH Program Project and Training Grants. Departmental faculty are members of the interdisciplinary Program in Neuroscience (**http://neuroscience.umaryland.edu**).

Successful candidates must have a Ph.D. or equivalent, evidence of productivity and innovation and an independently funded research program. For best consideration, applications should be received before **November 15, 2004**. Candidates should submit a detailed curriculum vitae, a statement of research interests and goals, and the names and addresses of three to five references. Electronic submission of all application materials (including supporting letters), as Microsoft Word file attachments to **facsearch@umaryland.edu**, is preferred. Paper applications may be mailed to:

Drs. Frank L. Margolis & Geoff Schoenbaum
Co-Chairs, Faculty Search Committee
Department of Anatomy & Neurobiology
University of Maryland School of Medicine
20 Penn Street
Baltimore, MD 21201
http://neurobiology.umaryland.edu

We are eager to diversify our faculty. Women and minorities are encouraged to apply. The University of Maryland is an AA/EOE/ADA Employer.

TEXAS TECH UNIVERSITY
SCHOOL OF MEDICINE

Professor and Chairperson
Department of Physiology

Texas Tech University School of Medicine invites applicants for the position of Professor and Chairperson of The Department of Physiology. The School of Medicine, which is primarily based in Lubbock Texas, has many outstanding professional and academic opportunities along with a growing research focus and is committed to expanding its research funding and infrastructure. The Department of Physiology is well equipped and has state-of-the-art imaging facilities. Chair candidates must possess a Ph.D. and/or M.D. degree. The chair must be dedicated to directing, promoting and developing the research and teaching missions of the department. Preferred candidates will have a current senior level rank in an accredited medical school with qualifications for appointment as a full professor. In addition, national and preferably international recognition in the field of Physiology is important. Knowledge and understanding of the organizational complexities of major academic institutions are highly desirable. The chairperson must possess excellent interpersonal skills and leadership qualities. Further information concerning the Department of Physiology can be accessed at **http://www.ttuhsc.edu/som/physiology/**.

Interested individuals should submit letters of application, C.V., and the names of three references either by regular mail or email to:

Mr. Bryce McGregor
Assistant Dean of the Medical School
Texas Tech University Health Sciences Center
Lubbock, Texas 79430
Email: bryce.mcgregor@ttuhsc.edu

TTUHSC is an Equal Opportunity Employer.

Molecular Systems Biology
Tenure Track Position in Mass Spectrometry or Chemical Biology
Center for Advanced Research in Biotechnology (CARB)

Applications are invited for a tenure-track faculty position at the level of Assistant, Associate, or full Professor. The successful applicant will be expected to develop a rigorous, externally funded research program using modern mass spectrometry or chemical approaches to study and manipulate biological processes at the molecular level. A competitive startup package will be provided.

CARB is developing an integrated program in molecular systems biology, to include components in chemical biology, mass spectrometry, structural biology, bioinformatics, experimental and computational biophysics, and systems modeling. Six new faculty hires are anticipated over the next two years, and a new research building equipped with state-of-the-art facilities is under construction and will open in 2005. We are particularly interested in applicants who are seeking a highly collaborative research environment.

A research center of the University of Maryland Biotechnology Institute and the National Institute of Standards and Technology, CARB has strong existing programs in areas that include macromolecular crystallography, high-resolution NMR spectroscopy, and experimental and computational molecular biophysics. See **www.carb.nist.gov** for further information.

Applications should include a curriculum vitae, a statement of research plans, and three letters of reference, sent to: **Chair, Faculty Search Committee (Position # 300491), Center for Advanced Research in Biotechnology, 9600 Gudelsky Drive, Rockville, MD 20850**. Review of applications will begin on **October 1, 2004** and will continue until a suitable candidate is selected.

The University of Maryland Biotechnology Institute is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and candidates with disabilities are encouraged to apply.

uOttawa

L'Université canadienne
Canada's university

Tenure-track positions, Faculty of Medicine
Department of Cellular and Molecular Medicine

The Department of Cellular and Molecular Medicine wishes to expand its strength in Computational and Systems Neuroscience. We are seeking dynamic individuals to fill several tenure-track positions at the junior or senior level. Strong candidates using innovative theoretical and experimental approaches to study neural function are encouraged to apply. These experimental approaches may range from the molecular to the systems level, but must be strongly coupled with computational modeling and theory. The ideal candidate will have an excellent track record of research that combines theory and experimentation, either within their own program, or in collaboration. Outstanding candidates will be eligible for Canada Research Chairs. Successful candidates will have the opportunity for cross-appointment with Departments in the Faculty of Science. They will also have the opportunity to interact with the large contingent of neuroscience researchers distributed throughout the Faculty of Medicine as well as within Federal government laboratories in Ottawa. Attractive start-up packages are available. Candidates will be expected to contribute to the teaching mission of the Department, including developing an interdisciplinary curriculum in Computational and Systems Neuroscience. Since the University of Ottawa is a bilingual institution, proficiency in both English and French would be an asset.

As Canada's National Capital, Ottawa is a vibrant and attractive city with a high standard of living. It has several cultural amenities and offers easy access to summer and winter outdoor activities.

Interested individuals are requested to submit a curriculum vitae, a list of at least three references and a statement of research interests to: **Dr. Bernard J. Jasmin, jasmin@uottawa.ca, Professor and Chair, Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, Canada K1H 8M5.** Applications will be reviewed until the positions are filled. More information on the Department can be obtained at: **http://www.uottawa.ca/academic/med/cellmed**.

All qualified candidates are encouraged to apply; however, Canadians and permanent residents will be given priority. Equity is a University of Ottawa policy; women, aboriginal people, members of visible minorities and persons with disabilities are invited to apply.

New York University

SENIOR FACULTY POSITION IN ORGANIC/BIOORGANIC CHEMISTRY

Department of Chemistry
FACULTY OF ARTS AND SCIENCE

As part of a continuing expansion of faculty and facilities, the Department of Chemistry at New York University invites applications for a senior level faculty appointment in organic chemistry, including organic materials/nanotechnology and bioorganic chemistry. Candidates should have demonstrated excellence in research and teaching. This opening is for a distinguished individual with an outstanding track record of funding and publications. Address correspondence to: **James Canary, Chair, Faculty Search Committee, Department of Chemistry, New York University, 100 Washington Square East, New York, NY 10003.** Please visit our website at: **http://www.nyu.edu/pages/chemistry**

NYU is an Equal Opportunity/Affirmative Action Employer.

POSITIONS OPEN

Harvard University: The Department of Psychology anticipates making one appointment at the **ASSISTANT** or **(UNTENURED) ASSOCIATE PROFESSOR** level to begin July 1, 2005, in the area of animal cognition. We are particularly interested in candidates focusing on such problems as decision making, cooperation, categorization, and spatial navigation, using either field or laboratory approaches, and with conceptual or practical links to problems in the neurosciences. The successful candidate will be expected to interface with Harvard's new initiative in the neurosciences and the new Center for Brain Sciences. Candidates with strong research and teaching interests in this area are invited to submit curriculum vitae and representative reprints to: **Chair, Department of Psychology, Harvard University, 33 Kirkland Street, Cambridge, MA 02138.** Candidates should ask three individuals familiar with their work to send letters of recommendation directly to the Chair of the Department. The closing date for applying is November 1, 2004. *Applications from women and members of minority groups are especially welcome. Harvard University is an Affirmative Action/Equal Opportunity Employer.*

Biochemistry. Oberlin College invites applications for a **TENURE-TRACK POSITION** beginning July 2005. Applicants must have a Ph.D. (or expected by December 2005) and a strong background in chemistry and biochemistry. Responsibilities include teaching biochemistry, general chemistry, and establishing a productive research program involving undergraduates. Oberlin is the undergraduate origin of more Ph.D.'s than any other liberal arts college. Entire description at **website: http://www.oberlin.edu/HR/FACopenings.** Send curriculum vitae, undergraduate and graduate transcripts, research plans, and have three letters of recommendation sent to: **Albert R. Matlin, Chair, Department of Chemistry and Biochemistry, Oberlin College, 119 Woodland Street, Oberlin, OH 44074,** by October 15, 2004. Late applications may be considered until position filled. *Affirmative Action/Equal Opportunity Employer.*

POSITIONS OPEN

NEUROSCIENCE ASSISTANT/ ASSOCIATE/PROFESSOR POSITIONS
University of Kentucky

The Department of Anatomy and Neurobiology announces the availability of two tenure-track positions at the **ASSISTANT, ASSOCIATE**, or **FULL PROFESSOR** levels. The positions are for individuals with outstanding research programs in translational neuroscience. Priority research areas for recruitment are neurodegenerative diseases, neural trauma, drug abuse, and NeuroAids. Applications are invited from creative, successful individuals who want to contribute to dynamic, growing research, and academic programs within a comprehensive Medical Center. Successful candidates are expected to develop and maintain innovative, nationally recognized research programs and/or academic programs. Competitive startup funds, salaries, and state-of-the-art facilities are available. Special consideration will be given to applicants who complement existing departmental strengths and who will significantly contribute to the department's teaching mission. Applicants must have a Ph.D. or M.D. or equivalent degree and should have two years of postdoctoral or other relevant experience. Interested individuals should send curriculum vitae, a summary of past experience, future research plans, and forward three letters of recommendation. Applications and nominations should be forwarded to: **Don M. Gash, Professor and Chair, Department of Anatomy and Neurobiology, 317 Whitney Hendrickson Building, (MRISC) University of Kentucky, Lexington, KY 40536-0098. E-mail: dongash@uky.edu. Website: http://www.mc.uky.edu/neurobiology/.** The Search Committee will begin reviewing applications on Monday, September 20, 2004, and will continue until the positions are filled. *Female and minority candidates are encouraged to apply. The University of Kentucky is an Equal Opportunity University.*

POSITIONS OPEN

MOLECULAR BIOLOGIST/GENETICIST

Oberlin College, Biology Department seeks individual with research interests in eukaryotic gene regulation for tenure-track position beginning fall 2005. Incumbent will teach in the cell and molecular biology curriculum required for biology majors, teach a comprehensive upper-level molecular genetics lecture and laboratory course, and may offer seminar for nonmajors in area of his/her interest. Entire description at **website: http://www.oberlin.edu/HR.** Requirements: Ph.D. (in hand by fall 2005); demonstrated interest and previous or potential excellence in undergraduate teaching. Postdoctoral experience desired. Submit statement of research and teaching interests, curriculum vitae, academic transcripts, and three letters of reference to: **Dr. Robin S. Treichel, Chair, Department of Biology, Oberlin College, Oberlin, OH 44074** by October 15, 2004. Late applications may be considered until position is filled. Direct questions to **e-mail: robin.treichel@oberlin.edu.** *Affirmative Action/Equal Opportunity Employer.*

The University of Oregon Psychology Department announces a search for a new tenure-track, **ASSISTANT** or **ASSOCIATE PROFESSOR POSITION** in systems neuroscience and/or behavioral genetics. Area of research interest is open, but we anticipate that the successful candidate will interact both with members of the Department and the Institute of Neuroscience. We are seeking active researchers who also are committed to excellence in teaching. Send curriculum vitae, a two to three page statement on research and teaching interests, reprints, and at least three letters of recommendation to: **Systems Neuroscience Search Committee, Department of Psychology, 1227 University of Oregon, Eugene, OR 97403-1227.** Deadline for submission is November 15, 2004. *The University of Oregon is an Equal Opportunity Employer/Affirmative Action/ADA Institution committed to cultural diversity.*

CASE
SCHOOL OF MEDICINE

MetroHealth

Case Western Reserve University
School of Medicine
Department of Reproductive Biology
MetroHealth Medical Center
CLEVELAND, OH

The Department of Reproductive Biology, Case Western Reserve University at MetroHealth Medical Center is seeking to solidify existing strengths in obesity/diabetes research by recruiting for full time position(s) for PhD or MD/PhD basic scientists at the rank of Assistant or Associate Professor level. Individuals conducting original research on the regulatory mechanisms of adipose tissue as an endocrine organ, homeostasis of the feto-placental unit, or other areas related to diabetes or obesity in relation to fetal growth, are encouraged to apply. Positions will be provided with a startup package, including laboratory space and access to molecular and cellular core facilities of the Rammelkamp Research and Schwartz Metabolism and Nutrition Research Centers.

To apply send curriculum vitae, letter of interest and names of at least three references (including email address and telephone) to: **shdemouzon @metrohealth.org**.

Sylvie Hauguel-de Mouzon, PhD
Director Molecular Research Division
Department OBGYN
MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland, OH 44109-1998
Phone: (216) 778-4876
Fax: (216) 778-1574

Patrick M. Catalano, MD, Professor and Chairman

MetroHealth Medical Center and Case Western Reserce Univeristy are Equal Opportunity/Affirmative Action Employers.

Sigfried and Janet Weis Center for Research, Geisinger Clinic

Senior Investigators in Cell Signaling

The Sigfried and Janet Weis Center for Research is seeking outstanding senior investigators in the area of cell signaling. Innovative and interactive individuals who complement existing strengths in G protein and growth factor signaling, extracellular matrix and membrane biology, and transcriptional regulation are preferred. Investigation can be carried out using cellular, molecular, genetic, or bioinformatics approaches.

Qualified applicants will have a Ph.D. and/or M.D. degree and a track record of significant independent research and external funding.

Send a CV, brief summary of research interests and plans, and names of three references to: Ms. Kristin Gaul, Administrative Secretary, Weis Center for Research, Geisinger Clinic, 100 N. Academy Avenue, Danville, PA, 17822-2600, or apply by email to kgaul@geisinger.edu.

www.geisinger.org/research

The Sigfried and Janet Weis Center for Research:

- **Highly interactive research institute environment**
- **Modern, well equipped laboratory facilities**
- **Opportunities for translational research collaboration with clinical investigators**
- **Generous start-up and ongoing research support**
- **Located in an attractive semi rural environment affording outstanding quality of life**

Geisinger
Heal. Teach. Discover. Serve.

FACULTY POSITIONS

ST. LAWRENCE UNIVERSITY

NEUROSCIENCE and BIOCHEMISTRY

Neuroscience – Tenure Track Position

The departments of Biology and Psychology at St. Lawrence University invite applications for a shared tenure-track position at the assistant professor level. We seek a neuroscientist with a Ph.D. who will contribute to a new dual track neuroscience major; one track being at the cellular level, the other being behavioral. The successful candidate will participate in teaching two neuroscience courses (Introductory and Advanced Neuroscience) and mentor senior research projects that are a requirement of the major. The successful candidate will be expected to use modern approaches to study the molecular - cellular basis of animal behavior and/or developmental neuroscience. There will also be the opportunity to develop an upper-level course in his/her area of expertise and to contribute to the introductory courses of either department as appropriate. We welcome applications from candidates who bring diverse cultural, ethnic and national perspectives to their scholarship and teaching. A demonstrated expertise in the use of computers and instructional technologies is also preferred.

Interested candidates should submit a letter of application, a curriculum vitae, a statement of teaching experience and philosophy that reflects innovative and progressive pedagogies, a statement of research interest, and have three letters of recommendation forwarded to: **Dr. T. Budd, Biology Department, St. Lawrence University, Romoda Drive, Canton, NY 13617**. Applications will be reviewed starting **September 15, 2004**. Later applications will be reviewed until the position is filled.

Biochemistry – Tenure Track Position

St. Lawrence University is searching for an individual with a Ph.D. in biochemistry, biological chemistry, or a related discipline. The departments of Biology and Chemistry have recently enacted a cooperatively administered interdisciplinary major in biochemistry. This will be a tenure track joint appointment at the assistant professor level. We welcome applications from candidates who bring diverse cultural, ethnic and national perspectives to their scholarship and teaching. The successful candidate will be expected to teach biochemistry, biochemistry research methods and help develop an interdisciplinary link between the departments at the introductory level. St. Lawrence University expects and is supportive of faculty mentored undergraduate research as a critical element of a liberal arts science education. The candidate will be expected to establish a productive research program to which undergraduates can actively contribute. All biochemistry majors participate in a senior research project. The two departments are currently engaged in the architectural planning and design of new research and teaching space. The departments house an impressive array of instrumental, microscopic and computational resources for the support of teaching and research. Details and additional information are available at our web sites (**http://it.stlawu.edu/~chem and http://it.stlawu.edu/~biol**).

Interested candidates should submit a CV, graduate and undergraduate transcripts, statements of teaching philosophy and research interest and plans and arrange for three letters of reference to be sent to: **Dr. T. Budd, Biochemistry Search Committee, Bewkes Hall, St. Lawrence University, Canton, NY 13617 (tbudd@stlawu.edu).** Completed applications will be reviewed beginning **October 24, 2004** and the search will continue until the position is successfully filled.

St. Lawrence University, chartered in 1856, is an independent, private, non-denominational university whose mission is to provide an inspiring and demanding undergraduate education in the liberal arts to students selected for their seriousness of purpose and intellectual promise. For more information please visit SLU's homepage at **http://web.stlawu.edu/resources/job.html**.

SLU is an AA/EO Employer.

THREE TENURE-TRACK BIOLOGY POSITIONS
Genetics, Plant Physiology, and Biology Education

Truman State University invites applications for three, tenure-track biology faculty positions, starting August 2005. Appointments are expected at the **ASSISTANT PROFESSOR** level for positions one and two and at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level for position three. Candidates should be strongly committed to the "teacher-scholar" model in a liberal arts and sciences institution and to maintaining both quality teaching and an active research program. To review a more detailed position announcement, please visit **website: http://www.truman.edu/pages/152.asp.** For more information about the University and the biology program, please visit **websites: http://www.truman.edu** and **http://biology.truman.edu.**

(1)Developmental genetics or bacterial genetics: to teach a sophomore-level genetics course and, depending on specialty, an upper-level course in either developmental biology or microbiology. Research area is open for both specialties. (2) Plant cell biology/physiology: to teach a sophomore-level cell biology course and a junior-level plant physiology course. We are especially interested in candidates whose research addresses cellular-level questions and who have broad training in plant biology. (3) Biology education/pedagogy: to coordinate and teach first-year biology courses, teach upper-level course(s) in area of specialty, conduct research in the area of biological education and pedagogy, and provide leadership in emerging undergraduate science education initiatives and funding opportunities. Good leadership and communication skills are essential for this position. We are especially interested in candidates with demonstrated experience in this area. Appointment at the Associate level will be considered for candidates with meritorious credentials and who have served at least five years in rank at the Assistant level.

Candidates should possess a Ph.D. by August 2005 (Ed.D. also considered for the introductory biology position). Complete applications include cover letter clearly indicating desired position, curriculum vitae, statements of teaching philosophy and research interests/goals (including an understanding of and support for the liberal arts and sciences), copies of all graduate and undergraduate transcripts, and three letters of reference. All application materials should be sent to: **Dr. Jeffrey Osborn, Search Committee (specify position), Division of Science, Truman State University, Kirksville, MO 63501-4221; telephone: 660-785-4017.** Review of complete applications will begin September 20, 2004, and continue until the positions are filled.

Truman is an Equal Employment Opportunity/Affirmative Action/ADA Employer.

Tufts University, Department of Chemistry, is seeking to expand its faculty with a tenure-track appointment at the **ASSISTANT PROFESSOR** level. Preference will be given to candidates whose research involves nanoscale materials, biomedical chemistry, or noncovalent interactions. Preference will be given to those whose research complements the department's strengths. The successful candidate will join a thriving Ph.D.-granting department, demonstrate the potential to develop an outstanding, internationally recognized research program, and excel in teaching. Teaching responsibilities include graduate courses in the candidate's discipline as well as undergraduate courses in chemistry. A Ph.D. in chemistry and postdoctoral experience are required. Additional information about the Department can be **found at website: http://chem.tufts.edu.** Send curriculum vitae, a research plan, and three letters of recommendation to: **Faculty Search Committee, Department of Chemistry, Tufts University, Medford, MA 02155.** Evaluation of candidates will begin October 11, 2004, and continue until the position is filled. *Tufts University is an Affirmative Action/Equal Opportunity Employer. We are committed to increasing the diversity of our faculty. Applications from women and members of underrepresented groups are strongly encouraged.*

POSITIONS OPEN

HAVERFORD

ASSISTANT PROFESSOR OF BIOLOGY
Haverford College

Haverford College seeks an evolutionary biologist with a cellular and molecular perspective for a new tenure-track position beginning fall 2005. The successful candidate will contribute to a vibrant, interdisciplinary, liberal arts curriculum and receive teaching credit for maintaining an active research program engaging undergraduate students. Applications are especially welcome from scholars applying evolutionary and/or computational approaches to areas in plant biology, developmental biology, the emergence and diversity of life, or comparative genomic analyses. At least two years of postdoctoral research experience required. Send letter of application, curriculum vitae, statements of research plans and teaching interests, and three current letters of reference by October 18, 2004, to: **Merleen Macdonald, Search Secretary, Haverford College, 370 Lancaster Avenue, Haverford, PA 19041-1392.** Questions to: **Jennifer Punt, Department Chair (e-mail: jpunt@haverford.edu).** *Haverford College* (**website: http://www.haverford.edu**) *is an Equal Opportunity/Affirmative Action Employer and is committed to diversifying its faculty and enriching its curriculum.*

ENDOWED PROFESSORSHIP at Michigan State University: The Michigan State University College of Osteopathic Medicine is seeking applications to fill the Walter F. Patenge Endowed Chair. The successful candidate will have demonstrated expertise conducting fundamental and/or translational neuromusculoskeletal research. The position is open to individuals with an outstanding record of funded research and peer-reviewed publication who possess an appropriate medical and/or research degree (e.g., Ph.D., Sc.D., D.O., M.D.). The successful applicant will have a background that demonstrates his/her ability to work synergistically with scientific and medical colleagues.

The position entails a tenured **ASSOCIATE** or **FULL PROFESSORSHIP** in the department(s) appropriate to the candidate's research interests, a salary commensurate with an endowed professorship, a suitable setup package, and annual interest from the endowment for furthering the candidate's research.

The position is open immediately and will remain posted until filled. Applications and nominations should include a letter of interest and current curriculum vitae to: **Chair, Michigan State University College of Osteopathic Medicine Endowed Chair Search Committee, c/o Kimberly Betts, Office of the Dean, Michigan State University College of Osteopathic Medicine, A309 East Fee Hall, East Lansing, MI 48824,** or **e-mail: bettski@msu.edu.** *Michigan State University is an Affirmative Action/Equal Opportunity Institution. Women and minorities are encouraged to apply.*

TENURE-TRACK BIOCHEMIST
St. Olaf College
Department of Chemistry

Tenure-track Biochemist at the **ASSISTANT** or **ASSOCIATE PROFESSOR** rank, starting September 1, 2005. Responsibilities include teaching courses in chemistry and biochemistry and contributing significantly to our interdisciplinary program in biomolecular science. Candidates should demonstrate a commitment to the goals of liberal arts education, including quality undergraduate teaching at all levels and building an experimental research program that involves undergraduates. Applicants must hold a Ph.D. degree in biochemistry or a closely related field or anticipate completing it before the starting date. Details at **website: http://www.stolaf.edu/depts/chemistry/biochemist.htm.** *A liberal arts college affiliated with the Lutheran Church (ELCA), St. Olaf College is an Affirmative Action/Equal Opportunity Employer and values diversity in its students, faculty, and staff. Applications by women and minorities are encouraged.*

POSITIONS OPEN

BIOANALYTICAL CHEMISTRY
University of Toronto

The Department of Chemistry, the Centre for Cellular and Biomedical Research (CCBR), and the McLaughlin Centre for Molecular Medicine (MCMM), University of Toronto, (**website: http://www.chem.utoronto.ca**) invites applications for a **JUNIOR POSITION** in bioanalytical chemistry, effective on or after July 1, 2005. Preference will be given to candidates with expertise in developing and deploying state-of-the-art analytical and spectroscopic techniques to study aspects of biological systems. The candidate should complement existing strengths and opportunities in biological and medicinal chemistry at the University of Toronto. The successful applicant will be nominated for a junior level (i.e., Tier II) Canada Research Chair (CRC). This position will be joint between chemistry and the CCBR (**website: http://ccbr.med.utoronto.ca/**) and MCMM (**website: http://www.mcmm.ca**). (For information on the CRC program, please see **website: http://www.chairs.gc.ca/.**) Applicants are expected to establish a research program in which international leadership in a field-of-study will be widely recognized. The successful candidate will be expected to conduct an active and innovative research program and to effectively teach courses at both the undergraduate and graduate levels in the departments. Salary will commensurate with qualifications and experience.

Applications will be accepted until October 1, 2004. Applicants should provide curriculum vitae, statement of teaching philosophy and interests, an outline of their proposed research, and should arrange to have three confidential letters of recommendation sent on their behalf to: **Chair of Chemistry, Department of Chemistry, University of Toronto, 80 St. George Street, Room 151 Toronto, Ontario M5S 3H6, Canada.** You may mail your material, to the address above, or **e-mail: chmsrch@chem.utoronto.ca.** If you are submitting electronically, only PDF documents will be accepted. *The University of Toronto is strongly committed to diversity within its community and especially welcomes applications from visible minority group members, women, Aboriginal persons, persons with disabilities, members of sexual minority groups, and others who may contribute to the further diversification of ideas. All qualified candidates are encouraged to apply; however, Canadians and permanent residents will be given priority.*

FACULTY POSITION
Cell Signaling and Cancer Biology

The Department of Molecular and Cellular Biology, Baylor College of Medicine is seeking an outstanding senior scientist for a joint position as a **TENURED PROFESSOR** in the Department and in the Cancer Center. Applicants should have a well-funded research program in cell signaling and expertise/interests that will contribute to the Cancer Center mission. By September 24, 2004, candidates should send their curriculum vitae, a statement of accomplishments, and future research plans, as well as a list of names and addresses for three references to: **Nancy L. Weigel, Ph.D., Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX 77030. E-mail: nweigel@bcm.tmc.edu.**

Affirmative Action/Equal Opportunity Employer.

CAREER IN OPTOMETRY, OPTOMETRIC RESEARCH, OR TEACHING

The New England College of Optometry offers a unique program for those with a Doctorate in the sciences: biology, chemistry, physics, psychology, pharmacology, medicine, etc. Candidates have the opportunity to obtain the Doctor of Optometry (O.D.) degree in 27 months. The program begins annually in early March. Employment opportunities exist in clinical practice, industry, optometric faculty positions, and research. **Contact: the Admissions Office, Department S, 424 Beacon Street, Boston, MA 02115. Telephone: 1-800-824-5526; e-mail: admissions@ne-optometry.edu. Website: http://www.ne-optometry.edu.** Application deadline: February 1, 2005.

Oak Ridge National Laboratory

Computing and Computational Sciences

The Oak Ridge National Laboratory (ORNL) in Tennessee is a leading center for basic and applied research in high-performance computing, computational sciences, systems engineering, intelligent systems, mathematics, and computer sciences. Our mission includes work on national priorities in advanced computing systems, work for U.S. government and industry customers to enable efficient and cost-competitive design, and work with universities to enhance science education and scientific awareness. Our researchers are finding new ways to solve problems beyond the reach of most computers and are putting powerful software tools into the hands of government and academic researchers and industrial scientists throughout the country.

DOE Leadership-Class Computing Facility for Science at ORNL

Energy Secretary Spencer Abraham announced on May 12 that Oak Ridge National Laboratory will build a leadership-class computing facility for science over the next five years at a total estimated cost between $150-$200 million. When finished, this computer will have a sustained capacity of 50 trillion calculations per second — or 50 teraflops — and more than 250 trillion teraflops per second at its peak.

Opportunities

Many new scientific and technical staff are needed now in specific initiatives or strategic research areas in the Computing and Computational Sciences Directorate. Opportunities also exist for joint tenure-based positions with our university partners (see http://www.ornl.gov/ornlhome/university_partners.shtml). We anticipate openings in the following research and applications areas:

- Ultrascale Computing and Simulation
- Visualization Research
- Architecture/Software Research
- Computer Science Research
- Computational Biology
- Computational Mathematics
- Computational Materials
- Computational Fusion (ITER)
- Computational Chemistry
- Computational Nanosciences
- Climate Research and Modeling
- Systems Engineering
- Complex Systems (Optical & Quantum Computing, Laser Arrays, Optical Radars, and High-Performance Networks)
- Networking Research
- Geospatial/Remote Sensing Science
- Energy Infrastructure Modeling
- Communications Infrastructure Modeling
- Cyber Security and Information Infrastructure Research

To apply for specific current job openings

To apply for specific current job openings, please visit: **http://computing.ornl.gov/Employment**

For additional information about these opportunities, please send an email, referencing a specific position of interest in your subject line, to: **CCSD_Staffing@ornl.gov**

ORNL, a multiprogram research facility managed by UT-Battelle, LLC, for the U.S. Department of Energy, is an equal opportunity employer committed to building and maintaining a diverse work force.

Office of Science
U.S. DEPARTMENT OF ENERGY

ORNL Center for Computational Sciences

TENURE-TRACK FACULTY POSITION IN EXPERIMENTAL BIOPHYSICS (ASSISTANT PROFESSOR/ASSOCIATE PROFESSOR/FULL PROFESSOR)
University of Arizona

The Department of Physics invites applications from outstanding candidates for a tenure-track faculty position in experimental biophysics, to start in the fall of 2005. The interdisciplinary search committee encourages applications from highly qualified candidates from any experimental research area in biological physics, broadly interpreted to cover a variety of research topics which may include but are not limited to biomolecular structure, function, and dynamics; networks, signaling, bio-sensors, and devices. Candidates should have a Ph.D. degree or equivalent, outstanding postdoctoral research accomplishments, and the ability to conduct an independent and vigorous research program. Commitment to excellence in teaching at all levels is expected. The position is anticipated to be at the Assistant Professor level, but senior appointments may be considered depending on qualifications and experience. The new faculty member will join an active interdisciplinary research environment in the College of Science at the University of Arizona. For further information, please visit **website: http://www.physics.arizona.edu/~biophys.** The Department is seeking an individual who is able to work with diverse students and colleagues, and who has experience with a variety of teaching methods and curricular perspectives.

To apply, please send curriculum vitae including a list of publications and a statement of research interests, and arrange to have at least three letters of recommendation sent to: **Search Committee, Experimental Biophysics, Department of Physics, University of Arizona, 1118 E. 4th Street, Tucson, AZ 85721.** Review of applications will start on November 15, 2004, and will continue until the position is filled.

As an Equal Opportunity/Affirmative Action Employer, the University of Arizona recognizes the power of a diverse community and encourages applications from individuals with varied experiences and backgrounds. The University of Arizona is an Equal Employment Opportunity/Affirmative Action, Minorities/Females/Persons with Disabilities/Veterans Employer.

ASSISTANT PROFESSOR OF BIOLOGY
Amherst College

The Department of Biology at Amherst College invites applications for a tenure-track position at the Assistant Professor level in some aspect of genomic biology. Areas of interest include, but are not limited to, comparative or functional genomics, protein structure and interactions, and metabolic relations. We especially desire candidates having an experimental research program that can involve undergraduate biology majors. Teaching duties include participation in a team-taught, introductory course that covers genetics, cellular, and molecular biology and includes a laboratory component, and two upper-level courses in the candidate's area, one with laboratory. A Ph.D. in biological sciences is required, and postdoctoral experience is expected. Send curriculum vitae and a statement of research and teaching interests to: **Genomic Biologist Search Committee, Department of Biology, Amherst College, Amherst, MA 01002-5000.** Have three letters of recommendation sent separately. Review of applications will begin October 18, 2004, and continue until the position has been filled. Further information on the Department can be found at **website: http://www.amherst.edu/~biology.**

Amherst College is a private undergraduate liberal arts college for men and women with 1,600 students and 165 faculty members. Located in the Connecticut River Valley of Western Massachusetts, Amherst participates with Hampshire, Mount Holyoke and Smith Colleges, and the University of Massachusetts in the Five-College Consortium.

Amherst College is an Equal Opportunity/Affirmative Action Employer and encourages women, persons of color, and persons with disabilities to apply. The administration, faculty, and student body are committed to attracting qualified candidates from groups presently underrepresented on our campus.

POSITIONS OPEN

University of Michigan Medical School

VIROLOGY FACULTY POSITION
Department of Microbiology and Immunology
University of Michigan Medical School

The Department of Microbiology and Immunology (**website: http://www.med.umich.edu/microbio/home.html**) is seeking an outstanding scientist in the area of virology for a tenure-track faculty position at the **ASSISTANT PROFESSOR** level (although candidates of all ranks will be considered). Applicants should have a Ph.D., M.D., or M.D./Ph.D. degree and relevant postdoctoral training. They will be expected to develop a vigorous externally funded research program and to contribute to the teaching mission of the Department. Significant scientific resources including a generous startup package and modern facilities will be available. Candidates who apply through this Department will also be considered for the University of Michigan Biological Scholars Program (**website: http://www.med.umich.edu/medschool/orgs/bssp/**). Applicants should e-mail a pdf file of their curriculum vitae and a statement of research interests to **e-mail: sherylhs@umich.edu.** Three letters of recommendation should be sent directly to**: Chair, Virology Search Committee, Department of Microbiology and Immunology, University of Michigan Medical School, 5641 Medical Science II, 1150 W. Medical Center Drive, Ann Arbor, MI 48109-0620.** Deadline for receipt of applications is November 1, 2004.

University of Michigan is an Equal Opportunity/Affirmative Action Employer committed to achieving diversity among its faculty and staff.

The Department of Pharmacology and Physiology at the University of Rochester Medical Center seeks applications for a full-time **TENURE-TRACK POSITION** at the rank of **ASSISTANT PROFESSOR.** Outstanding candidates qualified for higher ranks will also be considered. Competitive applicants will have a Ph.D. or equivalent degree, postdoctoral training, and a clear record of research productivity and creativity.

We are interested in applicants whose research program will complement existing faculty research strengths in cell signaling that include cell surface receptors, ion channels, G-proteins and calcium signaling, particularly in the fields of neuronal cell death, drugs of abuse and cardiovascular disease. The successful applicant will receive a competitive startup package and be expected to develop a dynamic, well-funded research program and contribute to graduate and medical teaching programs.

The University of Rochester Medical Center is undergoing a major expansion in basic and translational research. Additional information about the University, the Department and faculty research interests can be found at **website: http://www.urmc.rochester.edu/phph.**

Please send curriculum vitae, a brief statement of research plans, reprints of three key publications, and three letters of recommendation to: **Dr. A. William Tank, Chair, Search Committee, Department of Pharmacology and Physiology-Box 711, University of Rochester Medical Center, 601 Elmwood Avenue, Rochester, NY 14642.** *The University of Rochester is an Equal Opportunity Employer.*

BIOLOGIST. The Department of Biology at the University of San Francisco (USF) invites applications for a tenure-track position at the **ASSISTANT PROFESSOR** level, beginning August 2005, to teach upper-division courses in the field(s) of specialty, participate in lower-division courses for majors and nonmajors, and establish an active research program. For details, please see **website: http://www.usfca.edu/hr/employment/faculty3.html.** *USF is an Affirmative Action/Equal Opportunity Employer.*

POSITIONS OPEN

FACULTY POSITION IN MICROBIAL PATHOGENESIS

The Department of Medical Microbiology and Immunology, University of Alberta seeks applicants for a faculty position at the **ASSISTANT PROFESSOR** level. This position provides entry into the regular academic progression of the University, with the possibility of obtaining tenure. Areas of interest include (but are not limited to) research concerning microbial pathogenesis, host-pathogen interactions, and molecular pathogenesis. Applicants must have a proven record of research achievement and be competitive for external salary awards and research grants. We offer an outstanding research environment, which gives new researchers access to state-of-the-art equipment and modern laboratory facilities in a vibrant and supportive academic community (see **website: http://www.ualberta.ca/~mmi**). Successful candidates will be expected to develop dynamic research programs and devote 75 percent of their time to research while also contributing to undergraduate and graduate teaching. Remuneration will be commensurate with qualifications and experience. An attractive startup package, including three years of initial salary support, will be provided.

Individuals with a Ph.D. and appropriate postdoctoral training should submit curriculum vitae, a brief description of research plans, and the names of three individuals who may be contacted to provide a letter of reference by December 31, 2004, to: **Medical Microbiology and Immunology Search Committee, c/o Dr. D. Evans, Professor and Chair, Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Alberta T6G 2H7, Canada.**

All qualified candidates are encouraged to apply; however, Canadian citizens and permanent residents will be given priority. If suitable Canadian citizens and permanent residents can not be found, other individuals will be considered.

The University of Alberta hires on the basis of merit. We are committed to the principle of equity in employment. We welcome diversity in the workplace and encourage applications from all qualified women and men, including persons with disabilities, members of visible minorities, and Aboriginal persons.

FACULTY POSITION in Molecular Carcinogenesis. The Department of Chemistry and Biochemistry at Northern Arizona University (NAU) (**website: http://www.nau.edu/~chem/**) invites applications for a tenure-track position in molecular carcinogenesis at the **ASSISTANT** or **ASSOCIATE** level to begin August 2005. The successful candidate will be actively involved in the Native American Cancer Research Partnership with the University of Arizona (**website: http://www.nativecancer.org**). This position is initially funded by the National Cancer Institute and will involve a membership with the Arizona Cancer Center at the University of Arizona. Potential for collaboration also exists with the recently formed Translational Genomics Research Institute (**website: http://www.tgen.org**). The first two years of the position will involve no teaching requirements to allow the new faculty member to establish a strong graduate research program. Following this initial period, the individual will be expected to participate fully in the biochemistry curriculum at undergraduate and graduate levels. Qualifications include a Ph.D. in biochemistry or a related discipline, postdoctoral experience in cancer-related research, the ability to provide excellent instruction at the undergraduate and graduate levels and willingness to work with a culturally diverse population of faculty, staff, and students. A curriculum vitae, three letters of recommendation, a brief statement of teaching philosophy and commitment to Native American Student education, and proposed research directions should be sent to: **Chair, Molecular Carcinogenesis Search Committee, P.O. Box 5659, Northern Arizona University, Flagstaff, AZ 86011-5659.** The search will remain open until the position is filled; however, application review will begin on September 15, 2004. This position is subject to availability of funding. *NAU is an Equal Opportunity/Affirmative Action Institution. Minorities, Women, Persons with Disabilities, and Veterans are encouraged to apply.*

GSF – Research Center for Environment and Health, Munich

We are a national research center and a member of the Helmholtz Association financed jointly by the German Federal Government and the Federal State of Bavaria.

Our interdisciplinary research aims to identify health risks for man in his environment at an early stage, to elucidate mechanisms of disease and to develop concepts for prevention and therapy of diseases.

Our current priority areas within the framework of programme-based support from the Helmholtz Association in the Research Field "Health" are: "Environmental Health Disorders", "Comparative Genomics for Human Health", "Infection and Immunity", as well as smaller parts in "Cardiovascular and Metabolic Disease Research" and in "Cancer Research"; in the Research Field "Earth and Environment" we take part in the programme "Biogeosystems: Dynamics, Adaptation and Adjustment".

The researchers at the GSF in Neuherberg/Munich cooperate closely with the Ludwig-Maximilians-University and the Technical University Munich, with research institutions both in Germany and abroad, as well as with biotech firms. The center's current annual budget amounts to approximately € 150 million and the center has nearly 1600 members of staff.

The position of the

Scientific Director

is to be refilled as of the **August 1st 2005**.

The Scientific Director represents the center in scientific matters. His/her tasks include above all overseeing the scientific development and expansion of the center in the national and international research scene as well as research planning and the monitoring of success in cooperation with the center's executive bodies.

The suitable candidate will have an outstanding reputation in basic and clinical research. In addition, he/she should possess leadership experience in research management and his/her compelling personality combines creativity with integration skills and assertiveness.

The successful candidate will be appointed for a period of five years. Reappointment is possible. The salary will be based within the framework of that offered to high-ranking university professors.

The members of the Helmholtz Association are committed to increasing the proportion of women in leading positions. Therefore applications from women are particularly welcome.

Please send your application, together with all relevant documents within six weeks of the publication of this advertisement, to the Chairman of the Recruitment Commission at the following address:

An den
Vorsitzenden des Aufsichtsrats der GSF
Herrn Reinhard Junker
– persönlich –
im Bundesministerium für Bildung und Forschung
D-11055 Berlin, Germany

gsf

GSF–National Research Center
for Environment and Health
member of the Helmholtz Association

www.gsf.de

HELMHOLTZ GEMEINSCHAFT

Virginia Tech

DEPARTMENT HEAD
Plant Pathology, Physiology, and Weed Science

The College of Agriculture and Life Sciences invites applications for the position of Professor and Head of the Department of Plant Pathology, Physiology, and Weed Science. The Department has 26 faculty members, with outstanding research programs in molecular biology, functional genomics, and basic biology of plant-microbe interactions, plant-plant interactions, abiotic stress physiology, metabolic engineering, conventional plant protection approaches, and weed biology/management. A full position description and additional information on departmental programs is available at **website: http://www.ppws.vt.edu.** Applicants should complete a faculty application and submit complete curriculum vitae, a statement of intent, and names, addresses, and telephone numbers of five references online at **website: http://jobs.vt.edu.** Review will begin on October 1, 2004, and continue until the position is filled. Additional inquiries should be directed to: **Mr. Don Ball, Fralin Biotechnology Center, Virginia Tech,** at **e-mail: biotech@vt.edu** or by **telephone: 540-231-6934.**

Equal Opportunity/Affirmative Action Employer.

ASSISTANT PROFESSOR IN GENETICS OF NEURAL SYSTEMS AND BEHAVIOR
New Position at Caltech

We invite applications for a tenure-track **ASSISTANT PROFESSOR** appointment in the Division of Biology at the California Institute of Technology. We are seeking highly qualified candidates who are committed to a career in research and teaching. The applicant should conduct research at the interface of molecular biology and systems neuroscience aimed at understanding neural circuits and the control of behavior. We encourage applications from individuals working on vertebrate or invertebrate systems. The initial appointment term is four years, and appointment is contingent upon completion of all the requirements for a Ph.D.

Applicants should submit curriculum vitae, list of publications, a brief statement of research interests and teaching experience, and arrange for three letters of recommendation to be sent to:

Chair of Genetics of Neural Systems and Behavior Search
Division of Biology 216-76
California Institute of Technology
Pasadena, CA 91125

The California Institute of Technology is an Affirmative Action/Equal Opportunity Employer. Women, Minorities, Veterans, and Persons with Disabilities are encouraged to apply.

IMMUNOLOGIST

The College of the Holy Cross invites applications for a **TENURE-TRACK ASSISTANT PROFESSOR** in biology. An Immunologist will be hired to teach a laboratory course in immunology, a second upper-division course in an area compatible with current offerings, and a course for nonscience majors, and to develop a research program involving undergraduates. Supplementary areas of departmental interest include virology, neurobiology, and endocrinology. The successful candidate will hold a Ph.D. at the time of appointment. Holy Cross is a highly selective, exclusively undergraduate, Jesuit, liberal arts college (enrollment 2,700) that values excellence in both teaching and research. Applications, consisting of curriculum vitae, transcripts, copies of publications, research and teaching statements, and letters from three referees, should be submitted no later than 20 October 2004 to: **Dr. Cara Constance, Chair, Immunology Search Committee, Department of Biology, College of the Holy Cross, Worcester, MA 01610.**

The College is an Equal Opportunity Employer and complies with all Federal and Massachusetts laws concerning Equal Opportunity and Affirmative Action in the workplace.

POSITIONS OPEN

ASSISTANT OR ASSOCIATE PROFESSOR, NONTENURE RESEARCH TRACK
University of Pennsylvania School of Medicine
Department of Surgery
Division of Urology

The Department of Surgery at the University of Pennsylvania's School of Medicine seeks candidates for two Assistant or Associate Professor positions in the nontenure research track. Rank will be commensurate with experience. The successful applicant will have worked in the field of pathology, cell/molecular biology, or biochemistry. Responsibilities include targeted research in urologic oncology and utilization of a cell/molecular biological approach to investigate the mechanism for smooth muscle contractile dysfunctions. Applicants must have an M.D. and/or Ph.D. or equivalent degree.

The successful candidate will have demonstrated potential for establishing a vigorous independent research program in the cellular/molecular basis of diseases of the lower urinary tract. Preference will be given to candidates with experience in basic urological research. The effective date of appointment will be January 1, 2005. Please submit curriculum vitae, letter of interest, and references to:

Samuel K. Chacko, D.V.M., Ph.D.
Professor of Pathobiology
Chair, Search Committee
Division of Urology/Department of Surgery
University of Pennsylvania School of Medicine
3400 Spruce Street, 3005 Ravdin Courtyard
Philadelphia, PA 19104-4283

Ref. ad no. Urology research_0105

The University of Pennsylvania is an Equal Opportunity/Affirmative Action Employer. Women and minority candidates are strongly encouraged to apply.

PROFESSOR AND DIRECTOR, Mass Spectroscopy and Proteomics Research Facility: Case Western Reserve University School of Medicine intends to bring together and enhance its already strong mass spectroscopy and proteomics programs and facilities under the leadership of an established investigator with expertise in the field and interest in leading extensions of this technology to other researchers and schools at Case. Opportunities exist to create a state-of-the-art facility for highly specialized studies to supplement routine analytical capabilities already in place. We seek a forward-thinking established scientist with an active research program in the field, who will have the opportunity to recruit an operations director at the doctoral level for the day-to-day management of the core facility. The Director's appointment will be flexible with respect to home department. The Institution anticipates strong interactions among this program and growing programs in genetics and genomics, bioinformatics, and structural biology. Please send inquiries or curriculum vitae with three references by **e-mail to: pamela.davis@case.edu.** *In employment, as in education, Case Western Reserve University is committed to Equal Opportunity and Affirmative Action. Case is a recipient of a National Science Foundation ADVANCE Institutional Transformation Grant to increase the participation of women in Science and Engineering.*

PROFESSOR OF BIOLOGY

The Department of Biology and the Huck Institutes of Life Sciences at Penn State University invite applications for faculty appointments at the **FULL PROFESSOR** rank. We seek outstanding scientists in the area of molecular evolution whose research accomplishments are internationally recognized. Applications or letters of interest including curriculum vitae and a description of current research interests should be sent to: **Chair of Molecular Evolution Search Committee, Pos. #S-18314, 208 Mueller Laboratory, The Pennsylvania State University, University Park, PA 16802.** Review of applications will begin immediately and will continue until the positions are filled. *Penn State is committed to Affirmative Action/Equal Opportunity and the diversity of its workforce.*

POSITIONS OPEN

USDA ARS Agricultural Research Service
www.ars.usda.gov

The USDA, Agricultural Research Service, National Program Staff, Animal Production, and Protection Organization in Beltsville, Maryland, is seeking a National Program Leader for Genomics/Bioinformatics. This senior-level position directs research policies and programs for USDA's chief in-house science agency. The National Program Leader is responsible for developing the working agenda for a major genome research program on agriculturally important animals, plants, and microorganisms.

Candidates need an extensive background in bioinformatics and/or molecular biology and must have advanced research experience in one or more of the specialty areas. Recruitment is at the GS-14/15 levels. Salary commensurate with experience (GS-14, $85,000 to $110,000; GS-15, $100,000 to $130,000 per year plus benefits). This is a permanent, full-time position.

Candidates must be U.S. citizens. Application must address specific education and experience requirements. To request copy of vacancy announcement, **telephone: 301-504-1482** or go to **website: http://www.ars.usda.gov.** Click on Careers, under Current Job Openings, click on Scientists and Engineers, announcement # ARS-X4E-0336, opens August 23, 2004. Application must be postmarked by October 25, 2004. *USDA/ARS is an Equal Opportunity Employer and Provider.*

EVOLUTION AND SYSTEMATICS OF PLANTS AND FUNGI
University of Michigan

The Department of Ecology and Evolutionary Biology and the University Herbarium solicit applications for two tenure-track faculty positions in the evolutionary biology of plants or fungi. We seek accomplished individuals, with primary research interests in areas such as molecular systematics, phylogenetic theory, evolution of development, comparative genomics, or biodiversity informatics. We expect to hire at the **ASSISTANT PROFESSOR/ASSISTANT CURATOR** level, but interested senior candidates are encouraged to contact the search committee (**e-mail: plantsearch@umich.edu**). The successful candidates will also provide scholarly leadership in the use of the Herbarium's outstanding research collections. See **websites: http://www.eeb.lsa.umich.edu** and **http://herbarium.lsa.umich.edu** for more information. To apply, send curriculum vitae, statements of research and teaching interests and experience, evidence of teaching excellence, copies of publications, and arrange to have three letters of reference sent to: **Chair, Plant Evolution and Systematics Search Committee, Department of Ecology and Evolutionary Biology, The University of Michigan, 830 N. University, Room 2019S, Ann Arbor, MI 48109-1048.** Review of application materials will begin October 4, 2004. *Women and minorities are encouraged to apply. The University is supportive of the needs of dual-career couples. The University of Michigan is a nondiscriminatory, Affirmative Action Employer.*

INORGANIC CHEMISTRY SEARCH

California Institute of Technology invites applications for a tenure-track position as **ASSISTANT PROFESSOR** specializing in inorganic chemistry with an initial appointment of four years, contingent upon completion of all requirements for a Ph.D. in chemistry or other related field. Outstanding candidates with a strong commitment to research and teaching excellence are encouraged to apply. Submit curriculum vitae, publication list, a description of proposed research, and three letters of recommendation to: **Chair of the Inorganic Chemistry Search Committee, M/C 127-72, California Institute of Technology, Pasadena, CA 91125.** Applications should be received by October 18, 2004. *The California Institute of Technology is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and disabled persons are encouraged to apply.*

THE AFRICAN AGRICULTURAL TECHNOLOGY FOUNDATION

JOB OPPORTUNITIES

The African Agricultural Technology Foundation (AATF) is a new and unique not-for-profit foundation facilitating and promoting partnerships with public and private sector entities designed to remove many of the barriers that have prevented smallholder farmers in sub-Saharan Africa from gaining access to existing agricultural technologies that could help improve food security and reduce poverty in the continent. AATF's operations are based in Africa and are led, managed and directed by Africans. AATF is recruiting three outstanding individuals to fill senior positions at its headquarters in Nairobi, Kenya.

Position 1: Technical Operations Manager

Reporting to the Executive Director, the Technical Operations Manager will have responsibility for identifying appropriate opportunities for agricultural technology interventions to address the needs of resource-poor African farmers for food security and income generation; assessing the feasibility and probability of success of priority project concepts; identifying sources of appropriate technologies, negotiating modalities for accessing and coordinating activities for the deployment of such technologies in Africa; and providing overall leadership and technical supervision in the implementation of the AATF's project portfolio.

Suitable candidates must have a PhD in agricultural/biological sciences and over ten years of research and development experience; familiarity with new and advanced agricultural technology applications; understanding of the technical requirements of intellectual property rights management and technology licensing; experience in developing and managing projects spanning several African countries; demonstrated capacity to work and provide leadership within a collaborative framework, both with individuals and institutions, and within a multidisciplinary, multicultural setting; good communication, computer and interpersonal skills; fluency in written and spoken English or French with working knowledge of the second language; working knowledge of Portuguese will be an added advantage.

Position 2: Project Manager

Reporting to the Technical Operations Manager, the Project Manager will be responsible for the day-to-day implementation of AATF's project portfolio. Responsibilities will include the development of procedures and processes for appropriate consultations with a broad range of stakeholders to prioritize opportunities for interventions; the development of project business plans; and monitoring and technical supervision of individual technology transfer project and preparation of progress reports.

Suitable candidates must have a PhD in agricultural/biological sciences with at least five years' research experience; knowledge of new and advanced agricultural technology applications; knowledge/understanding of the technical requirements of intellectual property management and technology licensing; proven experience/skills in project development and management; demonstrated capacity to work within a collaborative framework both with individuals and institutions, and within a multidisciplinary, multicultural setting; good communication, computer and interpersonal skills; fluency in written and spoken English or French with working knowledge of the second language; working knowledge of Portuguese will be an added advantage.

Position 3: Regulatory Systems Specialist

Reporting to the Technical Operations Manager, the Regulatory Systems Specialist will be responsible for developing and managing the approval of agricultural products in sub-Saharan Africa and will take leadership in the development and management of essential components in the regulatory approval process for the deployment of agricultural technologies; provide leadership in ensuring compliance with regulatory requirements of countries where projects are implemented; advise partners and collaborators on regulatory aspects and technology testing issues related to AATF projects; and participate in all phases of project development and implementation.

Suitable candidates must have an MSc or PhD in biological or agricultural sciences with at least five years experience in the agricultural sector; proven experience as a professional scientist in either the public or private sector; proven record of managing regulatory application and approval of agricultural products; familiarity with food and environmental safety assessment procedures; proven experience/skills in agricultural market development and management; demonstrated capacity to work collaboratively both with individuals and institutions and within a multidisciplinary and multicultural setting; good communication, computer and interpersonal skills; fluency in written and spoken English or French with working knowledge of the second language; working knowledge of Portuguese will be an added advantage.

COMPENSATION AND TENURE: The salary for these positions is at an international level and is commensurate with experience. The compensation package includes a housing allowance, assistance with the education of children, family health insurance, a pension contribution and annual home leave. The initial period of contract is for 3 years, and is renewable subject to satisfactory performance.

APPLICATION PROCEDURES: Applicants should be from a Sub-Saharan African country and should submit a detailed curriculum vitae, a cover letter and the names of three referees who can provide confidential assessment of their capabilities to a Search Committee. All communications relating to applications for this position should be addressed to the **Administration and Finances Manager, AATF c/o The International Livestock Research Institute, Box 30709, Nairobi, Kenya** (e-mail address **m.tilahun@cgiar.org**). Applications should be received by **30 September 2004**. A final decision on the appointment is expected to be made by mid-November 2004.

AATF welcomes applications from any person who is a national of a Sub-Saharan African country, regardless of gender, nationality, race, religious persuasion or political beliefs.

FACULTY POSITIONS
University of Washington

The Department of Biology seeks applications for two tenure-track faculty positions at the **ASSISTANT PROFESSOR** rank. In exceptional circumstances, appointment at the **ASSOCIATE PROFESSOR** or **PROFESSOR** level may be considered for candidates who have demonstrated a commitment to mentoring underrepresented students in the sciences. Successful candidates should have completed at least one year of postdoctoral experience and will be expected to contribute to undergraduate and graduate teaching and to maintain an innovative and externally funded research program. Send curriculum vitae, a description of research and teaching interests, reprints of three recent publications, and three letters of reference to the appropriate address below.

Field Ecology: We seek applicants whose ecological research involves organisms in natural environments and includes a significant field component. Send application to: **Field Ecology Search Committee, Department of Biology, Box 351800, University of Washington, Seattle, WA 98195.**

Plant Functional Biology: We seek applicants investigating biochemical, cellular, developmental, or physiological mechanisms of plant function. Send application to: **Plant Biology Search Committee, Department of Biology, Box 351800 University of Washington, Seattle, WA 98195.**

Priority will be given to applications received before October 22, 2004. *The University of Washington is building a culturally diverse faculty and strongly encourages applications from women and minority candidates. The University of Washington is an Equal Opportunity/Affirmative Action Employer.*

FACULTY POSITION
Department of Molecular and Human Genetics

The Department of Molecular and Human Genetics at Baylor College of Medicine invites applications for a tenure-track position. We are seeking applications from outstanding individuals using genetic approaches and emerging concepts such as microRNA to study control of gene expression in eukaryotes with a special emphasis on cellular function and organ physiology. We will also consider outstanding applications in other areas. The research interests of the faculties in the Department of Molecular and Human Genetics range from bacterial to human genetics and from developmental biology to molecular physiology and pathophysiology of neurodegenerative diseases.

Candidates are expected to hold a Ph.D. or M.D. degree or equivalent and to have demonstrated outstanding achievement in their field. Applicant should submit curriculum vitae, a one to two page summary of research accomplishments, and a one to two page description of future research plans. Applicant should also have three letters of recommendation provided by November 1, 2004, to the Chair of the Search Committee. The address for submission of all materials is:

Gerard Karsenty, M.D., Ph.D.
Chair of Gene Expression
Faculty Search Committee
Department of Molecular and Human Genetics
Baylor College of Medicine
One Baylor Plaza
Houston, TX 77030

Baylor College of Medicine is an Equal Opportunity/Affirmative Action/Equal Access Employer.

POSTDOCTORAL POSITION for the study of chromatin dynamics in DNA damage and repair using yeast and mammalian cells (*Cell* **115:**537–549). Position begins April 4, 2005, for two years, with the possibility of extension, in the laboratory of: **Dr. Akash Gunjan** at **Florida State University, Department of Biomedical Sciences, Tallahassee, FL 32306, U.S.A.** Candidates with experience in molecular biology, chromatin, or yeast genetics can send curriculum vitae and three recommendation letters via **e-mail: akash.gunjan@cancer.org.uk.**

POSITIONS OPEN

ASSISTANT PROFESSORS IN TOXICOLOGY
Department of Biological Sciences

The Department of Biological Sciences and the Border Biomedical Research Center at the University of Texas at El Paso (UTEP) is seeking two tenure-track Assistant Professors starting July 1, 2005, for its expanding research emphasis in toxicology. Candidates that focus on biochemical toxicology, pharmacotoxicology, or chemical carcinogenesis are particularly invited, although all areas of toxicology will be considered. The Department (**website: http://academics.utep.edu/biology**) will occupy a new $30 million state-of-the-art facility in the fall of 2005, which includes mammalian and aquatic animal facilities, and core facilities in tissue culture, molecular biology, protein chemistry, microscopy, and DNA sequencing.

Qualifications Required: Applicants must have a Ph.D. and postdoctoral research experience. The successful candidates will develop and maintain a strong independent and extramurally funded research program and contribute to both undergraduate and graduate (M.S./Ph.D.) education.

Application Procedure: Applications should be sent to: **Toxicology Search Committee, Department of Biological Sciences, The University of Texas at El Paso, 500 W. University Avenue, El Paso, TX 79968-0519,** and should include curriculum vitae, a statement of research interests, copies of three publications, and contact information for three references. Applications will be reviewed beginning November 1, 2004. *The University of Texas at El Paso does not discriminate on the basis of race, color, national origin, sex, religion, age, disability, veteran's status or sexual orientation in employment or the provision of services.*

ENDOWED PROFESSORSHIP at Michigan State University: The Michigan State University College of Osteopathic Medicine is seeking applications to fill the Osteopathic Heritage Foundation Endowed Chair. The successful candidate will have demonstrated expertise conducting fundamental and/or translational research on the autonomic nervous system. The position is open to individuals with an outstanding record of funded research and peer-reviewed publication who possess an appropriate medical and/or research degree (e.g., Ph.D., Sc.D., D.O., M.D.). The successful applicant will have a background that demonstrates his/her ability to work synergistically with scientific and medical colleagues.

The position entails a tenured **ASSOCIATE** or **FULL PROFESSORSHIP** in the department(s) appropriate to the candidate's research interests, a salary commensurate with an endowed professorship, a suitable setup package, and annual interest from the endowment to further the candidate's research.

The position is open immediately and will remain posted until filled. Applications and nominations should include a letter of interest and current curriculum vitae to: **Chair, Michigan State University College of Osteopathic Medicine Endowed Chair Search Committee, c/o Kimberly Betts, Office of the Dean, Michigan State University College of Osteopathic Medicine, A309 East Fee Hall, East Lansing, MI 48824,** or **e-mail: bettski@msu.edu.** *Michigan State University is an Affirmative Action/Equal Opportunity Institution. Women and minorities are encouraged to apply.*

The Department of Chemistry of the University of Chicago invites applications from outstanding individuals for the position of **ASSISTANT PROFESSOR** of Chemistry. This search is in the areas broadly defined as inorganic, organic, and physical chemistry. Applicants should submit hard copies of curriculum vitae, a list of publications, and a succinct outline of their research plans. Candidates should arrange for three letters of recommendation to be sent to: **Michael D. Hopkins, Chairman, Department of Chemistry, The University of Chicago, 5735 S. Ellis Avenue, Chicago, IL 60637.** Review of completed applications will begin October 1, 2004. To ensure full consideration, all materials should be submitted by that date. *An Equal Opportunity/Affirmative Action Employer.*

POSITIONS OPEN

ASSISTANT PROFESSOR
BIOLOGICAL SCIENCES (GENETICS)

The Department of Biological Sciences at The University of Texas at El Paso (UTEP) seeks to fill a tenure-track Assistant Professor position in the area of evolutionary genetics. The successful candidate will develop and maintain a strong independent and extramurally funded genetics research program. Research resources at UTEP include molecular and cell biology core facilities in protein chemistry, DNA sequencing, tissue culture, and microscopy, a curated biosystematic collection of vertebrates, invertebrates, and plants, a 39,000 acre research station located in a relatively pristine Chihuahuan Desert landscape, and a biostatistics consulting facility.

Qualifications Required: Teaching and mentoring at both the undergraduate and graduate levels (M.S. and Ph.D.) are required. Applicants should have a research focus that combines molecular and field-based techniques, and be able to collaborate with other members of the Department.

Application Procedure: Candidates should send an application that includes curriculum vitae, a statement of research interests, a brief description of teaching philosophy and professional experience, and a list of three references with addresses and telephone numbers to: **Search Committee Chair (genetics), Department of Biological Sciences, The University of Texas at El Paso, El Paso, TX 79968-0519.** Review of complete applications will begin November 1, 2004. Visit the departmental **website: http://academics.utep.edu/biology.** *The University of Texas at El Paso does not discriminate on the basis of race, color, national origin, sex, religion, age, disability, veteran's status, or sexual orientation in employment or the provision of services.*

ASSISTANT/ASSOCIATE PROFESSOR
Southern Illinois University Cancer Institute

The Cancer Institute, Southern Illinois University School of Medicine at Springfield **(website: http://www.siumed.edu/cancer)**, announces the availability of two tenure-track positions at the level of Assistant/Associate Professor starting immediately. This institute is a newly developed comprehensive cancer center with state-of-the-art research facility. The successful candidate will possess a Ph.D. and/or M.D. degree and will be expected to develop a dynamic, extramurally funded research program in basic and/or translational cancer biology that will complement ongoing programs. Preference will be given to applicants with a strong background in molecular and cellular biology. Substantial startup packages and the opportunity for a joint appointment with an academic clinical department are available. Applicants should submit their curriculum vitae including a list of publications, a brief statement of research interests, and names of references to: **Kounosuke Watabe, Ph.D., Chair of the Search Committee, SIU Cancer Institute, School of Medicine, Southern Illinois University, P.O. Box 19626, Springfield, IL 62794-9626.** The deadline for receipt of applications is September 30, 2004. However, applications will be processed on an ongoing basis and we will interview potential candidates until the positions are filled. *SIU is an Equal Opportunity Employer. Women and minorities are encouraged to apply.*

BIOLOGICAL CHEMISTRY
Boston University

The Department of Chemistry invites applications for a **TENURE-TRACK ASSISTANT PROFESSORSHIP** in biological chemistry to commence in September 2005. The successful candidate will be expected to establish an innovative research program and to participate in the undergraduate and graduate teaching activities of the Department. Candidates should submit curriculum vitae, a description of proposed research, and arrange for three letters of recommendation to be sent to: **Professor Tom Tullius, Chair, Department of Chemistry, Boston University, 590 Commonwealth Avenue, Boston, MA 02215-2521.** The deadline for receipt of applications is November 1, 2004. *Boston University is an Equal Opportunity/Affirmative Action Employer.*

Department of Health & Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
Division of Intramural Research
Laboratory of Molecular Cardiology
Bethesda, Maryland

The Laboratory of Molecular Cardiology, NHLBI, is seeking a postdoctoral fellow who has obtained an M.D./Ph.D. within the past 2 years. This postdoctoral fellow will join an active program studying the role of nonmuscle myosin IIs in mouse and human embryonic development. Previous experience in developmental biology, cell biology, and molecular biology is desirable. The successful candidate will have a number of core facilities (microscopy, proteomic, imaging, transgenic, etc.) at their disposal and will be encouraged to develop their own approaches to understanding the role of nonmuscle myosins in mouse and human development and disease processes.

For more information, please consult our web page and PubMed or e-mail Dr. Robert S. Adelstein at: **AdelsteR@nhlbi.nih.gov.** Applicants should submit their C.V. and arrange for three letters of recommendation to be sent either to the above e-mail address or to:

Dr. Robert S. Adelstein
NHLBI/NIH
Building 10, Room 8N202
10 Center Dr MSC 1762
Bethesda, MD 20892-1762

Applications should be submitted by **October 31, 2004**.

DHHS and NIH are Equal Opportunity Employers. Applications from women, minorities, and persons with disabilities are strongly encouraged. The NHLBI/NIH is a smoke-free workplace.

Incyte is a Wilmington, Delaware-based drug discovery and development company with a growing pipeline of novel small molecule drugs to treat HIV, inflammation, cancer and diabetes. The company's most advanced product candidate, Reverset, is an oral, once-a-day therapy in Phase II clinical trials used to treat patients with HIV infections. Currently, Incyte has four drug discovery programs underway, an extensive intellectual property portfolio and a proteomic information business based in Beverly, Massachusetts.

Molecular Biologist

We are currently seeking a Molecular Biologist to join our **Wilmington, Delaware** team. In this role, the successful candidate will be relied upon to effectively interact within a multi-disciplinary molecular and cellular biology team, contributing to ongoing preclinical drug discovery and technology development projects. The position requires a BS/MS in a relevant field, at least 3 years experience in an academic or industrial laboratory setting, and expertise in molecular biology techniques, such as DNA/RNA isolation, PCR and RT-PCR. A background in quantitative real-time PCR and/or global transcriptional profiling is highly desirable.

For consideration, please send your resume to careers@incyte.com, referencing Job Code LL-RH. To learn more, please visit our website at www.incyte.com. Incyte Corporation is proud to be an Equal Opportunity Employer and recognizes the talent of its diverse workforce. EOE F/M/V

Incyte

Imagine Growing Together:
You and Monsanto
Imagine ideas growing through creativity and teamwork

The people of **Monsanto** are creating breakthroughs in science to improve both crop and animal agriculture around the world. We are currently seeking the following professionals to join our teams located in ***Davis, California, St. Louis, Missouri, and Mystic, Connecticut:***

PLANT BIOCHEMIST – Davis, California

We seek a talented scientist to contribute to our research on engineering metabolic pathways to improve seed oil in crop plants. You will join a multidisciplinary team to leverage genomics data to identify candidate genes, develop testing plans, and evaluate and optimize new and existing lead genes in transgenic crops. Requires a Ph.D. in Biochemistry, Plant Biology or related field with at least 2 years of postdoctoral experience. Demonstrated expertise with metabolic pathways, and experience in enzyme characterization are sought. Knowledge and/or experience in plant genetics, physiology and/or molecular biology are also desired. The successful candidate will have proven ability to conduct creative, high quality laboratory research, and will exhibit excellent communication and leadership skills that are required for our team-based work environment.

PLANT BIOCHEMIST – MOLECULAR BIOLOGIST – Davis, California

Conducting and coordinating research to improve oilseed crop seed composition through transgenic strategies, the selected candidate will apply standard techniques of DNA manipulation, such as DNA cloning and PCR methodology; analyze transgenic plants by enzyme assay, Western analysis, northern blotting and RealTime PCR; and participate in the development of scientific hypotheses and research plans. Requires a Ph.D. in Biochemistry, Genetics or a related field. Knowledge of metabolic pathways, a strong background in plant physiology and a basic knowledge of seed biology are desirable.

BIOCHEMIST – Davis, California

Lead a small team conducting research and development towards the genetic improvement of oil quality in a major crop as part of a larger multidisciplinary effort. Requires a Ph.D. in Biochemistry or related field and at least 1 year of postdoctoral experience; background in basic biochemical analytical methods, plant biology, protein purification and the development of enzyme assays preferred. Excellent communication and leadership skills are essential.

BIOCHEMIST/IMMUNOLOGIST – St. Louis, Missouri

We seek a Ph.D.-level scientist with at least 3 years of postdoctoral training or industrial experience and a strong biochemistry background in immunology and protein purification science. The focus will include the creation of novel immuno and biochemical assays for quantitative analysis of plant transgenic proteins and protein characterization. The person in this position will facilitate collaborative work between transgenic crop project teams and the analytical team. Excellent verbal and written communication skills are required.

BIOCHEMIST – Mystic, Connecticut

We seek a self-starter with a Ph.D. in Biochemistry or related field and a minimum of 2 years postdoctoral training to conduct and coordinate biochemical research efforts for a team dedicated to improving the nutritional qualities of corn through metabolic engineering. Knowledge of metabolic pathways and practical experience in protein purification and development of enzymatic analyses required with a background in Plant Biology beneficial. Excellent communication, organizational and leadership skills are essential.

To view more complete and detailed job descriptions of these exciting positions, please visit our website located at **www.monsanto.com** and respond online. We offer very competitive salaries and an extensive benefits package. Monsanto values diversity and is an equal opportunity employer M/F/D/V.

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ASSISTANT PROFESSOR (In Physiology)
BIOLOGICAL SCIENCES

The Department of Biological Sciences and the Border Biomedical Research Center at the University of Texas at El Paso is seeking one tenure-track Assistant Professor for fall 2005 for its expanding research emphasis in neurological and metabolic disorders. Candidates whose research focus is in endocrinology, developmental neuroscience, or metabolic physiology are particularly invited. The Department (**website: http://academics.utep.edu/biology**) will occupy a new $30 million state-of-the-art facility in the fall of 2005, which includes mammalian and aquatic animal facilities, and core facilities in tissue culture, molecular biology, protein chemistry, microscopy, and DNA sequencing.

Qualifications Required: Applicants must have a Ph.D. and postdoctoral research experience. The successful candidates will develop and maintain a strong independent and extramurally funded research program and contribute to both undergraduate and graduate (M.S./Ph.D.) education.

Application Procedure: Applications should be sent to: **Physiology Search Committee, Department of Biological Sciences, The University of Texas at El Paso, 500 W. University Avenue, El Paso, TX 79968-0519,** and should include curriculum vitae, a statement of research interests, copies of three publications, and contact information for three references. Applications will be reviewed beginning November 1, 2004. *The University of Texas at El Paso does not discriminate on the basis of race, color, national origin, sex, religion, age, disability, veteran's status, or sexual orientation in employment or the provision of services.*

FACULTY POSITION IN CHEMISTRY
Department of Chemistry
University of California, Berkeley

The Department of Chemistry at the University of California, Berkeley solicits applications for a faculty position beginning in the fall of 2005. Outstanding senior-level and junior-level applicants will be considered. Creative and energetic candidates who show extraordinary promise or accomplishment in research and teaching are specifically sought in the field of bioorganic chemistry; however, exceptional candidates in any area of chemistry will be considered. Junior-level applicants should send curriculum vitae and a proposed research program, and should arrange to have three letters of recommendation sent to: **Chair, Faculty Recruitment Committee, Department of Chemistry, University of California, Berkeley, CA 94720-1460.** Please refer references to the University of California statement on confidentiality at **website: http://www.chance.berkeley.edu/apo/evalltr.htm.** The deadline for receipt of applications is October 15, 2004. Application review will begin September 1, 2004. *The University of California is an Equal Opportunity/Affirmative Action Employer.*

FACULTY POSITIONS
Stem Cell Program
Children's Hospital Boston

Children's Hospital Boston, Stem Cell Program is seeking two outstanding scientists for **ASSISTANT PROFESSOR POSITIONS (TENURE TRACK).** A Ph.D. and/or M.D. are required. We are interested in candidates with an interest in stem cell biology and who are able to develop a significant and independent research program. For one position, an interest in cancer and stem cells is preferred.

Applicants should submit a cover letter, curriculum vitae, and a summary of current and proposed research programs, and arrange for three letters of recommendation to be sent to: **CHB, Stem Cell Program Search Committee, Attention: Vonda Shannon, Children's Hospital Boston, Stem Cell Program, 300 Longwood Avenue/Karp 08215, Boston, MA 02115.** Application review will begin September 15, 2004, and will continue until positions are filled.

Children's Hospital Boston is an Affirmative Action/Equal Employment Opportunity Employer. Qualified women and minority candidates are especially encouraged to apply.

POSITIONS OPEN

The Biology Department at Pomona College is seeking applications for a **TENURE-TRACK ASSISTANT PROFESSOR** in Computational Biology beginning fall 2005. We seek a biologist whose research and teaching interests include bioinformatic approaches. Areas of interest may include but are not limited to evolution, functional or comparative genomics, microbiology, cellular and molecular biology, physiological systems, and protein biochemistry/proteomics. The successful candidate will participate in teaching an introductory genetics course, develop and teach an upper-level bioinformatics course, contribute to departmental general education offerings, supervise senior theses, and establish an active research program involving undergraduates. We are particularly interested in candidates who have experience working with students from diverse backgrounds and a demonstrated commitment to improving access to higher education for disadvantaged students. The Biology Department is moving into new, state-of-the-art facilities. Competitive startup funds will be provided. Postdoctoral experience is preferred. Candidates should submit curriculum vitae, copy of graduate transcript, a statement of teaching philosophy including a description of the proposed bioinformatics course, a statement of research interests, reprints/preprints, and three letters of recommendation to: **Lenny Seligman (e-mail: lms14747@pomona.edu), Chair, Comp Bio Search Committee, Department of Biology, 609 N. College Avenue, Pomona College, Claremont, CA 91711-6339.** Complete applications received by October 15, 2004, will receive full consideration. *Pomona College is an Equal Opportunity Employer and especially invites applications from women and members of underrepresented groups.*

TENURE-TRACK FACULTY POSITION
Colorado State University

The Department of Biochemistry and Molecular Biology seeks applications for an **ASSISTANT PROFESSOR** with expertise in the molecular basis of infectious diseases. Candidates whose research interests complement existing departmental strengths are strongly encouraged to apply (please visit **website: http://www.bmb.colostate.edu** for research descriptions). Colorado State University is internationally recognized for research in infectious diseases and has close ties with several regional federal laboratories, including the Centers for Disease Control and Prevention and U.S. Department of Agriculture. This tenure-track position is part of a universitywide initiative to further broaden research on infectious diseases.

Qualifications include a Ph.D., postdoctoral experience, the ability to develop a productive, independent research program, and the potential to participate effectively in undergraduate and graduate teaching. Please submit application materials, including curriculum vitae and statements of research and teaching interests, online at **website: http://www.bmb.colostate.edu/jobs.cfm.** Three reference letters should be requested by the applicant and sent directly to **e-mail: jennifer.nyborg@colostate.edu.** Completed applications received by October 15, 2004, will be given full consideration. *Colorado State University is an Equal Employment Opportunity/Affirmative Action Employer.*

Biochemical/Pharmaceutical Engineering: Two full-time (academic year), tenure-track, joint appointments in the Faculty of Engineering and the College of Pharmacy at the University of Georgia: one at the **PROFESSOR/ASSOCIATE PROFESSOR** level and one at the **ASSISTANT PROFESSOR** level. See **website: http://www.engineering.uga.edu** for more information. Applicants should submit letter of application, curriculum vitae, statements of research/teaching plans, and contact information of four professional references to: **Dr. Mark A. Eiteman, Chair, Biochem/Pharm Engineering Search Committee, Driftmier Engineering Center, The University of Georgia, Athens, GA 30602-4435. E-mail: eiteman@engr.uga.edu.** To be assured full consideration, applications should be received by November 1, 2004. *Equal Opportunity/Affirmative Action Institution.*

POSITIONS OPEN

Caltech's Information Science and Technology Initiative invites applications for up to two tenure-track positions at the **ASSISTANT PROFESSOR** level. We are seeking highly qualified candidates committed to a career in research and teaching with a research focus in the engineering, mathematical, physical, biological, or economics aspects of information and computation. Possible home options include Applied and Computational Mathematics, Applied Physics, Computation and Neural Systems, Computer Science, Control and Dynamical Systems, and Electrical Engineering, with possible joint appointments outside Engineering and Applied Science in Divisions such as Biology, Physics, Mathematics and Astronomy, or Humanities and Social Sciences. Candidates interested in all aspects of the interplay between biology and information science and technology are especially encouraged to apply.

Initial appointments at the Assistant Professor level are for four years and are contingent on completion of the Ph.D. degree. Exceptionally qualified applicants at the **ASSOCIATE** or **FULL PROFESSOR** level are also encouraged to apply. **POSTDOCTORAL POSITIONS** are also available.

Candidates are directed to the web pages at **website: http://www.ist.caltech.edu/joinus/positions.html** for instructions on how to apply online. Electronic (pdf) copies of your curriculum vitae (including a list of your publications), a statement of teaching and research plans, and three published manuscripts (pdf) are required as part of the application.

Caltech is an Equal Opportunity/Affirmative Action Employer. Women, Minorities, Veterans, and Persons with Disabilities are encouraged to apply.

BIOCHEMISTRY
University of South Carolina

The Department of Chemistry and Biochemistry invites applications for two **TENURE-TRACK BIOCHEMISTRY POSITIONS** at the **ASSISTANT PROFESSOR** level. Applications for a more advanced position from well-qualified candidates will also be accepted. All areas of biochemistry will be considered but multidisciplinary candidates who would support current growth of the Department in the areas of cancer biochemistry, structural biology, and/or nanoscience are especially encouraged to apply. The candidate is expected to establish a vigorous, externally supported research program and have a strong commitment to teaching biochemistry at the undergraduate, graduate, or medical school levels. Applicants should submit a letter of application, curriculum vitae, a statement of research plans and teaching interests, and arrange for three letters of recommendation to be sent by November 15, 2004, to: **Chair, Biochemistry Search Committee, Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208.** Departmental information is available at **website: http://www.chem.sc.edu.** *The University of South Carolina is an Equal Opportunity/Affirmative Action Employer.*

EUKARYOTIC DNA REPAIR / GENOME STABILITY

The Department of Biochemistry and Biophysics and the Wilmot Cancer Center at the University of Rochester Medical Center invite applications for a tenure-track position in eukaryotic DNA repair and genome stability at the **ASSISTANT PROFESSOR** level or higher. Applicants employing genetic methods in mammalian systems are preferred, but those in areas complementing existing strengths in cell signaling, cancer cell biology, and biochemistry of DNA repair and chromatin are also invited. Submit curriculum vitae, a statement of research accomplishments and plans, and letters of recommendation to: **Robert Bambara, Repair Search, Box 712, University of Rochester Medical Center, 601 Elmwood Avenue, Rochester, NY 14642.** See **websites: http://dbb.urmc.rochester.edu** and **http://www.stronghealth.com/services/cancer** for details. *The University of Rochester is an Equal Opportunity/Affirmative Action Employer.*

UNIVERSITY OF MICHIGAN

BIOLOGICAL SCIENCES SCHOLARS PROGRAM
For Junior, Tenure-Track Faculty

The University of Michigan announces recruitment for the Biological Sciences Scholars Program (BSSP) to continue to enhance its investigational strengths in the life sciences research programs.

Now entering its 8th year, this Program has led to the recruitment of outstanding young scientists in the areas of genetics, microbiology, immunology, virology, structural biology, pharmacology, biochemistry, molecular pharmacology, stem cell biology, physiology, cell and developmental biology, and the neurosciences. The Program seeks individuals with PhD, MD, or MD/PhD degrees, at least two years of postdoctoral research experience, and evidence of superlative scientific accomplishment and scholarly promise. Successful candidates will be expected to establish a vigorous, externally-funded research program, and to become leaders in departmental and program activities, including teaching at the medical, graduate, and/or undergraduate levels. Primary college and department affiliation and rank will be determined by the applicant's qualifications and by relevance of the applicant's research program to departmental initiatives and focus. Preference will be given to appointments at the Assistant Professor level, though outstanding applicants at a more advanced career stage will also be considered.

Please apply to the Program through the BSSP web site at: http://www.med.umich.edu/medschool/orgs/bssp/. A curriculum vitae (including bibliography), a three-page Research Plan and three original letters of support should all be submitted through the BSSP web site.

More information about the Biological Sciences Scholars Program, instructions for applicants and those submitting letters of recommendation, and how to contact us is located on the BSSP web site: http://www.med.umich.edu/medschool/orgs/bssp/. The final deadline for applications is October 15, 2004.

The University of Michigan Medical School is an Affirmative Action/Equal Opportunity Employer

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Canada's Top 100 Employers 2004

Boehringer Ingelheim (Canada) Ltd.

ADME/PK Scientist (Ph.D.) – Biological Sciences Department

Boehringer Ingelheim is an innovative research-based pharmaceutical company with a global R&D network. The R&D centre of Boehringer Ingelheim (Canada) Ltd., located in the greater Montréal area, is a leader in antiviral drug discovery. Our research programs are directed toward the discovery and development of new medicines for the treatment of serious and life threatening viral diseases.

We have a career opportunity within our Biological Sciences Department for the following position:

ADME/PK Scientist (Ph.D.): SCB-648-05

We are seeking an ADME/PK scientist to work in close collaboration with multidisciplinary drug discovery teams (molecular and structural biologists, pharmacologists and medicinal chemists) to identify novel therapeutic agents for the treatment of HCV and HIV infections. Successful candidates will be responsible for ADME/PK studies in support of our research projects.

Candidates must possess at least 2 years of relevant post-doctoral experience, excellent scientific publication record, clear leadership potential, strong verbal and written communication skills, and an ability to work effectively in a team-based environment. An in-depth knowledge of pharmacokinetics is essential. Scientists with expertise in modern ADME/PK and bioanalytical technologies are particularly encouraged to apply. Knowledge of French would be an asset.

We provide a stimulating and challenging work environment and highly competitive compensation and benefits.

Should you be interested in this position, please forward your curriculum vitae to:

O Human Resources Department
Boehringer Ingelheim (Canada) Ltd.
Research & Development

2100, Cunard Street, Laval, Québec H7S 2G5
Fax: (450) 682-8434
E-mail: hr@lav.boehringer-ingelheim.com

Web Site: www.boehringer-ingelheim.ca

* We are actively committed to employment equity.

Boehringer Ingelheim

ASSISTANT PROFESSOR–ASTROBIOLOGY
University of Florida/Kennedy Space Center

The Department of Microbiology and Cell Science at the University of Florida invites applications and nominations for a 12-month tenure-track position as Assistant Professor to develop an internationally recognized research program in space life sciences related to the search for extraterrestrial life, microbial evolution in novel space-associated environments, or other aspects of astrobiology. Applicants must have a Ph.D., postdoctoral experience, and a strong publication record in relevant areas. The successful candidate is expected to develop an outstanding research program supported with extramural funding, to supervise Ph.D. students, and to be an innovative instructor of undergraduate and graduate students in microbiology and related areas in molecular biological sciences. The successful candidate will join a group of faculty with similar research interests located at the new Space Life Sciences Laboratory, Kennedy Space Center. Details of the Department and the position may be found at **website: http://microcell.ufl.edu.** Electronic applications only will be accepted (submit as a single pdf file). Applications should be sent to: **Professor Wayne Nicholson (e-mail: wln@ufl.edu)** and include a cover letter, curriculum vitae, and description of research interests. Applicants should also arrange to have three letters of reference sent directly to Professor Nicholson by e-mail. All application materials are due 15 October 2004 for a position starting 1 July 2005. *The University of Florida is an Equal Opportunity Employer.*

TENURE-TRACK POSITIONS in Biochemistry. Applications are invited for two tenure-track positions in biochemistry, one each in the Departments of Biology and Chemistry at the level of **ASSISTANT PROFESSOR** beginning fall 2005. We seek applicants who are committed to excellence in teaching at the undergraduate level and who are dedicated to developing an active research program that engages students in research. More details on both positions are available at **website: http://www.macalester.edu/provost/positions.html.** To apply for the position in biology, send a letter, curriculum vitae, statements of teaching philosophy and research plans, and three letters of reference to: **Professor Lin Aanonsen, Chair, Department of Biology, Macalester College, St. Paul, MN 55105.** To apply for the position in chemistry, send all of the above plus undergraduate and graduate transcripts to: **Professor Thomas D. Varberg, Chair, Department of Chemistry, Macalester College, St. Paul, MN 55105.** Applications received by October 15, 2004, will receive first consideration. Macalester College is a selective, private liberal arts college in the Minneapolis-St. Paul metropolitan area. The College prides itself on providing support for excellence in teaching and in faculty scholarship. *Macalester is an Equal Opportunity/Affirmative Action Employer and is committed to diversity. We are especially interested in candidates committed to working with students of diverse backgrounds.*

BIOLOGIST, ASSISTANT PROFESSOR TENURE TRACK, Ph.D. required, 16 August 2005. The University of South Carolina Aiken (USCA) is a predominantly undergraduate institution with a strong emphasis on teaching and research. The Department of Biology and Geology has a history of independent, funded research programs often involving undergraduates. We seek a biologist with expertise in eukaryotic cell biology, developmental biology, or physiology to complement existing departmental strengths. Teaching duties include human physiology and specialty area. Send letter of application, curriculum vitae, and contact information of three references to: **Dr. A. J. Dennis, Chair, Search Committee, Department of Biology and Geology, University of South Carolina Aiken, Aiken, SC 29801-6309.** Complete applications received by 15 October 2004 will receive full consideration. **Website: http://www.usca.edu/biogeo/search.html.**

Women and minorities are encouraged to apply. USCA is an Affirmative Action/Equal Opportunity Employer.

POSITIONS OPEN

MOLECULAR AND INTEGRATIVE PHYSIOLOGY
University of Michigan

We seek two new faculty members to join an interactive contemporary department focused around understanding the function of organisms across multiple levels of organization. One position at the **ASSISTANT PROFESSOR** level aims to recruit an individual studying membrane channels or transport molecules which can be related to integrative physiology or disease. This individual will also be considered for appointment as a Biological Scholar at the University of Michigan. The other position is open at any rank but senior appointment will require a strong history of external research support. Areas the Department is interested in developing include integrative genomics, islet beta cell function, biogerontology, and systems biology but all areas of physiology will be considered. Both positions require a doctoral degree and postdoctoral training and will involve participation in the teaching of graduate and professional students. Applicants should send (electronically or by mail) curriculum vitae, summary of research accomplishments and future plans, and arrange for three letters of reference to be sent to:

Dr. John A. Williams, Chair
Molecular and Integrative Physiology
7744 Medical Science II
University of Michigan
Ann Arbor, MI 48109-0622
E-mail: jawillms@umich.edu

The University of Michigan is an Equal Opportunity Employer committed to achieving diversity among its faculty and staff.

ORGANIC CHEMISTRY
Dartmouth College

Applications are invited for a faculty position at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level starting July 2005. The Chemistry Department seeks an individual who will establish a nationally recognized research program in organic chemistry at Dartmouth and who will excel at teaching in our undergraduate and Ph.D. curricula. Preference will be given to individuals with a strong background in physical organic chemistry. Appropriate areas may include bioorganic chemistry, organic materials, or catalysis. Candidates will be expected to teach introductory and advanced courses in organic chemistry, as well as graduate courses in their area of research. Applicants should submit curriculum vitae, a description of their research plans, and a brief statement about their teaching interests. Applicants should also arrange to have three letters of recommendation sent on their behalf. All inquiries and applications will be treated confidentially. Application materials should be sent to: **Chair, Organic Chemist Search Committee, Department of Chemistry, Burke Laboratory, Dartmouth College, Hanover, NH 03755-3564.** The Committee will begin to consider completed applications on October 15, 2004. *With an even distribution of male and female students and over a quarter of the undergraduate student population members of minority groups, Dartmouth is committed to diversity and encourages applications from women and minorities. Dartmouth College is an Equal Opportunity and Affirmative Action Employer.*

FACULTY POSITION IN NEUROSCIENCE/BIOCHEMISTRY

The Department of Biomedical Sciences at Marquette University invites applications for a tenure-track faculty position at the level of **ASSISTANT PROFESSOR.** The successful candidate will be expected to develop an independent, extramurally funded research program that expands the departmental research focus in neuroscience. A strong background in biochemistry is preferred. Send curriculum vitae, description of research interests, and the names of three references to: **Search Committee, Department of Biomedical Sciences, Marquette University, P.O. Box 1881, Milwaukee, WI 53201-1881.** Review of applications will begin in October 2004 and continue until the position is filled. *Affirmative Action/Equal Opportunity Employer.*

POSITIONS OPEN

FACULTY POSITION IN CANCER BIOLOGY

The Center for Cancer Research and Department of Biology at the Massachusetts Institute of Technology seek applicants for an appointment at the level of **ASSISTANT PROFESSOR (TENURE TRACK)** in the area of cancer biology. Areas of emphasis include, but are not limited to, oncogene and tumor suppressor gene function; signal transduction; intercellular communication; control of genome stability; cancer genetics, genomics, and proteomics; tumor immunology; cell adhesion, migration, and metastasis; angiogenesis; and stem cell biology and differentiation in vertebrate systems. The appointment will require supervision of an active research program as well as undergraduate and graduate teaching.

Applicants should include curriculum vitae, brief summaries of past accomplishments, and future research plans. Letters of recommendation should be sent separately from three scientists who can provide an evaluation of the candidate's accomplishments and future potential for both research and teaching.

Applications and letters should be sent to:

Cancer Biology Search Committee
E17-110, Center for Cancer Research
Massachusetts Institute of Technology
Cambridge, MA 02139

Deadline for receipt of applications and support materials: November 15, 2004.

MIT is an Affirmative Action/Equal Opportunity Employer. Qualified women and minority candidates are especially encouraged to apply.

FACULTY POSITION
Plant/Microbial Chemistry

The Department of Chemistry at Simon Fraser University (SFU) invites applications for a **TENURE-TRACK ASSISTANT PROFESSOR POSITION** in the area of Plant/Microbial Chemistry to take effect in September 2005, subject to final budgetary approval.

Applicants should have a Ph.D. degree and will normally have postdoctoral or industrial experience. Outstanding candidates with a commitment to excellence in research and teaching are being sought. The candidates will be expected to develop and maintain both an innovative, externally funded research program, and an excellent teaching record at both the undergraduate and graduate levels.

Applicants should send a complete resume, a research proposal, and a list of three individuals willing to act as references with their addresses, telephone and/or fax numbers, and e-mail addresses. All correspondence should be sent to: **Professor Andrew J. Bennet, Chair, Department of Chemistry, Simon Fraser University, 8888 University Drive, Burnaby, B.C., Canada V5A 1S6.** The competition will remain open until the position is filled. Screening of applications will commence on November 3, 2004. *All qualified candidates are encouraged to apply; however, Canadians and permanent residents will be given priority. Simon Fraser University is committed to an equity employment program that includes special measures to achieve diversity among its faculty and staff. We therefore particularly encourage applications from qualified women, Aboriginal Canadians, persons with disabilities, and members of visible minorities.*

The Department of Ecology and Evolutionary Biology, Tulane University, invites applications for two **TENURE-TRACK POSITIONS,** one in evolutionary systematics and one in plant ecology, at the level of **ASSISTANT PROFESSOR.** See **website: http://www.tulane.edu/~eeob/faculty_search.html** for details on each position. Send curriculum vitae, statements of research and teaching interests, selected publications, and names and addresses of three references to: either **Evolutionary Systematist Search** or **Plant Ecologist Search** at the **Department of Ecology and Evolutionary Biology, 310 Dinwiddie Hall, Tulane University, New Orleans, LA 70118-5698.** Review of applications will begin October 14, 2004, and the searches will remain open until the positions are filled. *Tulane University is an Affirmative Action/Equal Employment Opportunity Employer.*

MIDWEST RESEARCH INSTITUTE

Midwest Research Institute announces the search for a

DIRECTOR
for the Department of Energy's NATIONAL RENEWABLE ENERGY LABORATORY
Golden, Colorado

The President and Board of Directors of Midwest Research Institute (MRI) invite nominations and applications for the position of Director of the National Renewable Energy Laboratory (NREL) and Senior Vice President of Midwest Research Institute. NREL is a Federally Funded Research and Development Center (FFRDC) and is the Office of Energy Efficiency and Renewable Energy's primary national laboratory for renewable energy and energy efficiency research and development. NREL is managed for the U.S. Department of Energy (DOE), through its Golden Field Office, under a performance-based management and operating contract with MRI. Battelle teams with MRI in the management of the Laboratory. The appointment will be effective on November 1, 2004, or at a mutually agreeable date.

The Laboratory was established in 1977, and is located on a 325-acre site in Golden, Colorado. The Laboratory also operates the National Wind Technology Center on a 305-acre site between Golden and Boulder, Colorado. NREL's mission is to develop renewable energy and energy efficiency technologies and practices, advance related science and engineering, and transfer knowledge and innovations to address the nation's energy goals.

The Director is responsible for the management of the Laboratory and reports to the President and CEO of MRI, who Chairs the NREL Governing Board. Within MRI policy, the Director exercises broad delegated powers in the overall leadership of the Laboratory's programs and operations, including definition of their technical aspects, negotiation of their size and content, and execution of them to the highest quality. In addition, the Director ensures a strong infrastructure and workforce for the Laboratory, and an integrated safety and security management program. The Director has significant financial, human, equipment, and facility resources, with a Laboratory annual budget in excess of $200 million and a staff of approximately 1,150 scientists, engineers, and support personnel. Many of the NREL staff have joint university faculty appointments.

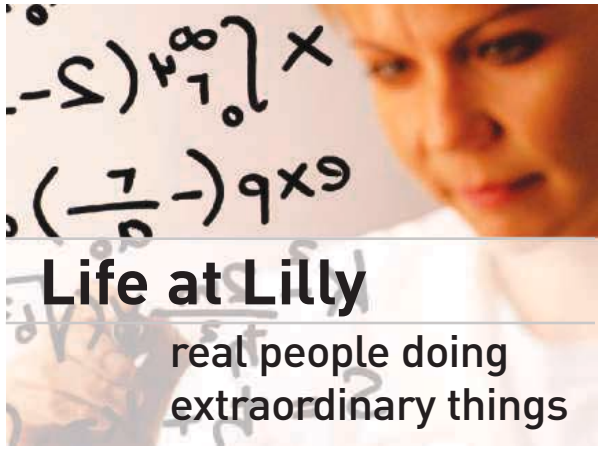
The Director is responsible for leading the Laboratory's programs for new energy technology development and research in basic and applied sciences, including its scientific and support centers and offices. NREL is home to the DOE's National Center for Photovoltaics, National Bioenergy Center, and the National Wind Technology Center, and is also the Systems Integrator for the President's Hydrogen Initiative. The Laboratory also participates in numerous national and international collaborations and public-private partnerships with industry in developing and transferring energy technologies. The Laboratory fosters science and engineering education, nationally and in the local community. All the research done at NREL is unclassified.

Candidates should have demonstrated success in leading and managing large scientific and technology programs or organizations; an extensive record of scientific and/or engineering accomplishments; and experience in transferring technology, knowledge, and innovations to the private sector. Salary is commensurate with experience.

MRI is conducting this search using the services of Heidrick & Struggles, Inc. Applications, accompanied by current resumes, may be sent to:

Mr. Randy Jayne
Senior Partner
Heidrick & Struggles, Inc.
1750 Tysons Blvd, Suite 300
McLean, Virginia 22101
rjayne@heidrick.com

NREL is an Equal Opportunity/Affirmative Action Employer.



Lilly is about breakthrough medicines and treatments to confront many of the most challenging diseases. As a leading, innovation-driven pharmaceutical corporation employing more than 41,000 employees worldwide, we know that the best way to find the next generation of drugs is to use the next generation of technology. And, at our new Systems Biology Center in Singapore, we're doing just that. While the rest of the industry anticipates the next generation of science, at Lilly, that's where you'll begin.

At Lilly Systems Biology in Singapore, you will work as part of a multidisciplinary team, focused on delivering solutions for drug discovery via bioinformatics and systems biology.

The following position is offered to candidates who are willing to relocate to Singapore.

Laboratory - Head, Biology

You will be involved in the set-up and management of a high-content (RNAi, microarray, etc.) biology laboratory focused on target and biomarker identification and validation. In addition, you will be responsible for staffing of laboratory, setting up and running assays and experiments. You will be part of the senior leadership team of Lilly Systems Biology and will work in close collaboration with scientists in the discovery research and bioinformatics groups in Singapore and Indianapolis. You are expected to play a key role in managing the scientific aspects of collaborations with external partners.

Along with a PhD in Molecular or Cell Biology, you should have at least 3 to 5 years of experience in managing a laboratory within the pharmaceutical or biotech industry. You must also possess demonstrated experience with large scale use of RNAi and microarray experiments. Fluency in state-of-the-art molecular and cell biology techniques is required, while experience in lab automation and/or medium throughput cellular assay screening is desired. Background in oncology is an advantage.

Please send your resumes, in strict confidence, to: lsb_recruitment_sg@lilly.com. Alternatively, resumes can be mailed to: The HR Manager, Lilly Systems Biology Pte. Ltd. 1 Science Park Road, #04-01, The Capricorn, Singapore Science Park II, Singapore 117528.

Qualified candidates who are interested in other Bioinformatics, IT or Biology positions are also invited to visit our website.

www.lsb.lilly.com

Lilly

Answers That Matter.

TWO TENURE-TRACK ASSISTANT PROFESSOR POSITIONS
Molecular Biology and Developmental Biology
Brandeis University

The Brandeis Department of Biology is seeking to fill two tenure-track positions in the following areas of research in mammals and other metazoans: (1) transcriptional regulation and/or chromatin structure-function, (2) molecular genetics of development. We seek to complement existing strengths in gene regulation of normal and cancer cells, development and function of the nervous system, or chromosome structure and function. We are particularly interested in candidates who use transgenic approaches. Candidates for appointment at the Assistant Professor level should have a Ph.D. or equivalent degree and postdoctoral experience. Exceptional candidates at a more advanced rank may be considered. Applicants should submit curriculum vitae and a detailed research plan and arrange for three letters of recommendation to be sent to:

Molecular and Developmental Biology Search Committee
MS 008, Department of Biology
Brandeis University, 415 South Street
Waltham, MA 02454-9110

First consideration will be given to candidates whose applications are received by October 15, 2004. *Brandeis University is an Equal Opportunity Employer, committed to building a culturally diverse intellectual community, and strongly encourages applications from women and minorities.*

FACULTY POSITION in Structural Biology, Department of Biochemistry and Molecular Biology, SUNY Upstate Medical University. The Department of Biochemistry and Molecular Biology is seeking applications to fill a tenure-track **ASSISTANT PROFESSOR** position. The successful applicant will be expected to develop well-funded research program and to contribute to medical and graduate teaching. Special consideration will be given to candidates using structural techniques to examine macromolecular complexes. Individuals whose research complements existing strengths in the Department in structural biology, bioenergetics, genomics, yeast genetics, and vertebrate gene expression are especially encouraged to apply. The successful candidate will receive a highly competitive startup package. Further information about the Department can be found at **website: http://www.upstate.edu/biochem.** Candidates should have a Ph.D. and/or an M.D. degree, postdoctoral experience, and a strong publication record. Applicants should submit curriculum vitae, a summary of their research accomplishments and future research plans, and arrange to have three letters of reference sent to: **Richard Cross, Ph.D., Chair, Department of Biochemistry and Molecular Biology, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210.** Review of applications will begin on November 1, 2004, and continue until the position is filled. *Women and minorities are encouraged to apply. Upstate Medical University is an Equal Opportunity/Affirmative Action Employer.*

The Department of Chemistry at the University of Louisville invites nominations and applications for the newly created position of **BLOCH PROFESSOR OF CHEMISTRY** and **DIRECTOR of the Institute of Molecular Diversity and Drug Design.**

The position requires an active, funded research program as well as effective teaching in the organic division of our graduate and/or undergraduate programs. In addition to the Chemistry Building, the Chemistry Department will expand to occupy part of a new, multidisciplinary Research Building that is scheduled to open in fall 2005. See **websites: http://www.louisville.edu/a-s/chemistry/** and **http://www.imd3.org.** Consideration of applications will begin October 1, 2004, and continue until the position is filled. Please send curriculum vitae, statement of interests, and contact information for three references to: **George Pack, Chair, Department of Chemistry, University of Louisville, Louisville, KY 40292.** *Women, African-Americans, and other minorities are strongly encouraged to apply.*

POSITIONS OPEN

McMaster University
HEALTH SCIENCES

CANADA RESEARCH CHAIR
in Inorganic Chemistry

The Department of Chemistry at McMaster University invites applications for a tenure-stream **FACULTY POSITION** in any area of inorganic chemistry, at any level. The successful candidate will hold a Ph.D. in chemistry, preferably with relevant postdoctoral experience, and will be expected to develop a strong externally funded research program and participate fully in teaching at both the undergraduate and graduate levels. Junior candidates will be considered for nomination for a Tier 2 Canada Research Chair.

The Department has superb structural characterization facilities, including magnetic resonance (NMR at 200 through 700 MHz), mass spectrometry and X-ray diffraction, and has just completed a period of active expansion and renovation of both its research and undergraduate teaching facilities.

Applications, including curriculum vitae, research proposal, statement of teaching interests/accomplishments, and letters from three references should be sent before September 30, 2004, to: **Dr. Brian E. McCarry, Chair, Department of Chemistry, McMaster University, Hamilton, ON, Canada L8S 4M1. Telephone: +1-905-525-9140, extension 24504; fax: +1-905-522-2509.**

All qualified candidates are encouraged to apply; however, Canadian citizens and permanent residents will be considered first for this position. McMaster University is committed to employment equity and encourages applications from all qualified candidates, including women, members of visible minorities, Aboriginal persons, members of sexual minorities, and persons with disabilities.

TENURE-TRACK POSITION IN NEUROPHARMACOLOGY

The Department of Pharmacology at Tulane University Health Sciences Center seeks an **ASSISTANT PROFESSOR.** Candidate should have a Ph.D., productive postdoctoral research experience, and an ability to develop innovative and extramurally funded research programs. The position offers newly renovated laboratory space, an outstanding scientific research environment, an excellent startup package, and access to graduate students in several successful programs, including pharmacology, interdisciplinary neuroscience, and interdisciplinary molecular and cellular biology. Individuals studying neurological disease at the molecular and system levels are especially encouraged to apply. Please send your curriculum vitae, statement of research interests, and the names and e-mail addresses of at least three references to:

Dr. Krishna C. Agrawal, chairman
Department of Pharmacology
Tulane University Health Sciences Center
1430 Tulane Avenue, SL 83
New Orleans, LA 70112
E-mail: agrawal@tulane.edu

Tulane is an Equal Opportunity Employer offering generous fringe benefits.

University of Rochester. The Department of Chemistry invites applications for a position at the **ASSISTANT PROFESSOR** level in any area of experimental chemistry. Exceptional candidates at the senior level may also be considered. Candidates are expected to establish an outstanding program of original research and be effective teachers at the graduate and undergraduate levels. Applicants should send curriculum vitae, a statement of research plans, and arrange for three letters of recommendation to be sent to**: Chemistry Faculty Search Committee, c/o Betty Stahl, Department of Chemistry, University of Rochester, RC Box 270216, Rochester, NY 14627-0216.** Review of applications will begin on October 15, 2004. *The University of Rochester is an Equal Opportunity Employer. Women and minority candidates are strongly encouraged to apply.*

POSITIONS OPEN

FACULTY POSITION
Pharmaceutics/Pharmacology

The Department of Pharmaceutical Sciences at North Dakota State University (NDSU) invites applications for a tenure-track position at the rank of **ASSISTANT/ASSOCIATE PROFESSOR,** rank based on qualification and experience. The appointment is expected to begin on or after July 1, 2005. Candidates must possess a doctoral degree in pharmaceutical/medicinal chemistry, pharmacology, pharmaceutics, or closely related fields, have at least two years of postdoctoral experience with a strong record of scholarship, and possess good interpersonal as well as effective oral and written communication skills. Preference will be given to those applicants with expertise in pharmaceutical chemistry, drug metabolism, pharmacokinetics, gene and protein delivery, or molecular pharmacology; to individuals whose research interests complement other departmental strengths; and to individuals with a degree in pharmacy. The successful candidate will be expected to establish an externally funded research program, teach and mentor graduate students, as well as participate in courses offered in the Pharm.D. curriculum. A competitive salary and a startup package are available. Additional information concerning the Department, the University, and Fargo can be obtained at **website: http://www.ndsu.edu/pharmsci/.**

Application deadline is October 15, 2004, or thereafter until the position is filled. The application portfolio containing curriculum vitae, statement of teaching philosophy, description of research interests and future plans, and the names and contact information for three references should be submitted to: **Dr. Stefan Balaz, North Dakota State University College of Pharmacy, Fargo, ND 58105.**

NDSU is an Equal Opportunity/Affirmative Action Employer.

THE PENNSYLVANIA STATE UNIVERSITY

Penn State DuBois and Penn State Hazleton, campuses of Pennsylvania State University's Commonwealth College, invite applications for biology faculty positions starting August 2005. Penn State DuBois seeks one **FACULTY MEMBER** for a multiyear appointment to teach introductory anatomy, physiology, pathophysiology, biology of aging, and microbiology courses. Penn State Hazleton seeks one **TENURE-TRACK FACULTY MEMBER** to teach human anatomy, physiology, and general survey biology courses. Required: Ph.D. in biology. Prior college-level teaching experience preferred. Evidence of a promising record of research (tenure-track). Visit **website: http://cwchome.psu.edu** for more information about the positions, campuses, and college. Application: Submit cover letter, resume, and the names, addresses, telephone numbers, and e-mail addresses of three references to: **Commonwealth College Faculty Searches, The Pennsylvania State University, 111 Old Main, Box SCI, University Park, PA 16802.** Applications also will be accepted as Microsoft Word or PDF files at **e-mail: cwcsearch@psu.edu.** Application review begins November 15, 2004, and continues until a suitable candidate is found. *Affirmative Action/Equal Opportunity Employer.*

ASSISTANT PROFESSOR, BIOLOGY
Mercer University in Macon, Georgia

Mercer University seeks a tenure-track Assistant Professor for August 2005 with a Ph.D. in biological sciences, broad training in genetics and molecular biology, and promise of excellence in teaching and scholarly activity. Candidates should be able to contribute to general science education and/or the University's interdisciplinary studies programs. Membership in Phi Beta Kappa is considered an advantage. Duties will consist of teaching five undergraduate courses per academic year, including introductory biology, genetics, and upper-division specialty. Research involving undergraduates is encouraged. Interested candidates should submit an online application at **website: http://www.mercerjobs.com.** *Affirmative Action/Equal Opportunity Employer/ADA.*

NCCN National Comprehensive Cancer Network®

Oncology Scientist/ Medical Writer

The National Comprehensive Cancer Network (NCCN), the authoritative, scientific source for evaluative information on appropriate cancer care, is seeking a motivated individual for the position of Scientist/ Medical Writer for the NCCN Drugs and Biologics Compendium. Successful candidate will work with NCCN expert panels and NCCN Guidelines to develop content for the Compendium. Individual will have MD, PhD, or PharmD and experience in oncology. Excellent writing skills are a must. Individual must possess ability to understand and evaluate medical literature, to abstract information concisely, and to work to deadlines. This position presents a unique opportunity with a premier organization in a significant growth phase. We offer competitive salary and excellent benefits.

Send CV/resume and salary history to: **HR, NCCN, 500 Old York Road, Suite 250, Jenkintown, PA 19046 or fax to (215) 690-0282. E-mail: jobs@nccn.org.**

EOE.

No calls please.

Case Western Reserve University
School of Medicine
Department of Reproductive Biology
MetroHealth Medical Center
CLEVELAND, OH

A postdoctoral training position is available to study regulatory mechanisms in pathophysiology of pregnancy and fetal development. The models are based mainly on longitudinal studies performed throughout normal and diabetic pregnancies. Mechanisms of altered insulin resistance are analyzed at the cellular and molecular levels on adipose tissue and skeletal muscle biopsies. Methods such as DNA microarrays, gene expression, organ cultures, proteomics are utilized. The MHMC campus offers a wide array of training opportunities including a strong clinical and basic science environment with access to basic core facilities as well as human clinical-translational research programs.

Applicants must have a strong background in molecular and cellular biology. They should be close to obtaining a Ph.D. degree or have less than 2-3 years of postdoctoral experience. Stipend is commensurate with experience. Please send a CV, a letter of interest and names of three references with e-mail addresses to: **Sylvie Hauguel-de Mouzon, PhD, Director Molecular Research Division, Department OBGYN, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, OH 44109-1998; Phone: (216) 778-4876; shdemouzon@metrohealth.org.**

Patrick M. Catalano, MD,
Professor and Chairman

MetroHealth Medical Center and Case Western Reserve University are Equal Opportunity/ Affirmative Action Employers.

National Research Council Canada | Conseil national de recherches Canada

NRC is a dynamic, nationwide R&D organization committed to helping Canada realize its potential as an innovative and competitive nation.

Institute for Marine Biosciences (IMB) Halifax, Nova Scotia Canada

The NRC Institute for Marine Biosciences (http://imb-ibm.nrc-cnrc.gc.ca) is respected worldwide for its research and technology development in marine biosciences. IMB features a broad and integrated suite of marine bioscience and biotechnology laboratories and a marine research station. IMB's research programs focus primarily on the areas of fish and shellfish aquaculture, natural toxins and mass spectrometry-proteomics. IMB is also home to the Canadian Bioinformatics Resource, a distributed bioinformatics computing environment and help desk available to biologists across Canada. The Institute also has a substantial suite of state-of-the-art advanced instrumentation in mass spectrometry– proteomics, high-throughput DNA sequencing, NMR and microscopy.

IMB requires Research Officers to develop creative, world-class research programs in the following areas:

Functional Genomics Research Officer
in cell and molecular biology, using functional genomics approaches to address aspects of fish or shellfish biology relevant to aquaculture.

Phytoplankton Biology Research Officer
in phytoplankton ecology/biology focused primarily on harmful marine microalgae.

Analytical Chemistry Research Officer
in the field of organic analytical chemistry. The focus of this position is the development of analytical methods and certified reference materials for phycotoxins.

For further information and application instructions, refer to: www.nrc-cnrc.gc.ca/careers

NRC·CNRC

Canada

FACULTY POSITION
Department of Biochemistry and Molecular Biology
Uniformed Services University of the Health Sciences
F. Edward Hébert School of Medicine

We invite applicants for a tenure-track position at the level of **ASSISTANT PROFESSOR.** The Department is seeking an outstanding individual capable of establishing and maintaining an independent and vigorous research program. Research interests in all areas of biochemistry and molecular biology will be considered. Applicants are required to have a Ph.D. degree in biochemistry, molecular biology, or a related field, and they must have postdoctoral experience and a clear potential to establish a strong and competitive research program. Applicants must also have a commitment to teaching graduate and medical students. Additional information about the Department and the Uniformed Services University of the Health Sciences can be obtained by accessing **websites: http://bio.usuhs.mil** and **http://www.usuhs.mil,** respectively.

Applicants should submit curriculum vitae, a concise description of future research plans, and arrange to have three letters of recommendation sent to: **Dr. Teresa Dunn, Faculty Search Committee, Department of Biochemistry and Molecular Biology, Uniformed Services University of the Health Sciences, F. Edward Hébert School of Medicine, 4301 Jones Bridge Road, Bethesda, MD 20814-4799.** All inquiries should be directed to **e-mail: psener@usuhs.mil.** Review of applications will begin November 15, 2004, and the search will continue until the position is filled. *The Uniformed Services University of the Health Sciences is an Equal Opportunity/Affirmative Action Employer.*

FACULTY POSITION: The Department of Neurology at Louisiana State University Health Sciences Center (LSUHSC), Shreveport, Louisiana, has an opening for a tenure-track faculty member to undertake the key position in the multiple sclerosis (MS)/neuroimmunology clinical and basic science projects. The appointment will be at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level, for a board-certified neurologist with a demonstrated pioneering research background in multiple sclerosis. The position requires internationally recognized expertise in demyelinating and neurodegenerative diseases. The applicant must have an established record as Principal Investigator on major grants in the field and must have expertise in developing independent research protocols in MS to obtain scientific grants. The applicant must have substantial publications in peer-reviewed professional journals in the field of multiple sclerosis. The candidate will conduct MS clinical trials and will continue research in abnormalities of cerebral endothelial cells in MS. This position offers a competitive income plus a comprehensive benefits package. The Department of Neurology at Louisiana State University Health Sciences Center is a tertiary referral center for North Louisiana and East Texas. Please send curriculum vitae and three reference letters to: **Roger E. Kelley, M.D., LSUHSC-Neurology, 1501 Kings Highway, Shreveport, LA 71130; e-mail: rkelly@lsuhsc.edu.** *We are an Equal Opportunity/Affirmative Action Employer.*

POSTDOCTORAL POSITION
Harvard Medical School

Postdoctoral position to study leukocyte trafficking using molecular biology, in vitro live cell fluorescence imaging, and transgenic mice models in Center for Excellence in Vascular Biology, Brigham and Women's Hospital. Requires recent Ph.D., M.D., M.D./Ph.D., and strong background in molecular biology, intracellular signaling, and developing transgenic mice models of inflammation. *Preference given to U.S. citizen or eligible to work in U.S.A.* Send curriculum vitae, brief description of research, and names of three references to: **Dr. Bill Luscinskas, Brigham and Women's Hospital, Boston, MA** at **e-mail: fluscinskas@rics.bwh.harvard.edu.** *We are an Equal Opportunity Employer.*

POSITIONS OPEN

FACULTY POSITION IN CELL/TISSUE ENGINEERING
Johns Hopkins University School of Medicine
Department of Biomedical Engineering

The Johns Hopkins University Department of Biomedical Engineering invites applications for a tenure-track faculty position in the general area of cell and tissue engineering, with a particular interest in application of microfabricated structures. Appointments at all academic levels will be considered. The successful candidate's primary appointment will be in the Department of Biomedical Engineering (**website: http://www.bme.jhu.edu/**) of the School of Medicine, and he/she will be a member of the Whitaker Biomedical Engineering Institute (**website: http://www.wbmei.jhu.edu**) and the Institute for Basic Biomedical Sciences (**website: http://www.bs.jhmi.edu**). These newly formed Institutes provide a highly interactive environment in which multidisciplinary teams of engineers, biologists, computer scientists, and mathematicians address biomedical problems of fundamental importance. The Whitaker Institute builds on internationally recognized research programs based in the School of Medicine and the Whiting School of Engineering. New faculty will be based in the School of Medicine and will have access to the facilities in Clark Hall, a recently completed Institute facility on the Homewood Campus of Johns Hopkins University. Successful applicants will be expected to establish independently funded research programs, and will participate in the graduate and undergraduate educational activities of both the Department of Biomedical Engineering and the Institutes.

In order to ensure full consideration, applications should be received no later than December 1, 2004. Interested applicants should send curriculum vitae, names of three references, and a statement of future research goals to:

Dr. Murray Sachs
Whitaker Biomedical Engineering Institute
The Johns Hopkins University School of Medicine
720 Ross Research Building
720 Rutland Avenue
Baltimore, MD 21205

The Johns Hopkins University is an Equal Opportunity/Affirmative Action Employer. Women and minorities are strongly encouraged to apply.

COMPUTATIONAL CHEMISTRY AND BIOPHYSICS
Boston University

The Department of Chemistry invites applications for a **TENURE-TRACK ASSISTANT PROFESSORSHIP** in theoretical and computational chemistry and biophysics to commence in September 2005. The successful candidate will be expected to establish an innovative research program and to participate in the undergraduate and graduate teaching activities of the Department. This position is part of a campus-wide initiative to develop interdisciplinary research in computational science in association with the Center for Computational Science and the Graduate Program in Bioinformatics at Boston University. Candidates should submit curriculum vitae and a description of proposed research, and arrange for three letters of recommendation to be sent to: **Professor Tom Tullius, Chair, Department of Chemistry, Boston University, 590 Commonwealth Avenue, Boston, MA 02215-2521.** The deadline for receipt of applications is November 1, 2004. *Boston University is an Equal Opportunity/Affirmative Action Employer.*

FACULTY POSITION IN A CARIBBEAN MEDICAL SCHOOL

Saint James School of Medicine is hiring faculty with teaching experience in any of the basic medical science subjects (pathology, microbiology, anatomical sciences, pharmacology, biochemistry) for its campus in the Caribbean (Bonaire). Teaching experience in the United States is desirable. Senior applicants may apply for the position of **ACADEMIC DEAN.** Please send resumes to **e-mail: career@sjsm.org** or **telephone: 1-800-542-1553** for more information (**website: http://www.sjsm.org).**

POSITIONS OPEN

ASSISTANT PROFESSOR OF BIOLOGY

Penn State Erie, The Behrend College, invites applications from invertebrate or cellular physiologists for a tenure-track position. Applicants must have a strong commitment to undergraduate teaching and research. Ph.D. is required; postdoctoral and teaching experience is a plus. Expectations: teach upper-division physiology courses with laboratories (two, in alternate years), a lecture course in biochemistry, share teaching responsibility for a core course in the biology major, establish a research program involving undergraduates, and seek external funding. Competitive startup funds are available.

Penn State Behrend is a four-year and graduate college of Penn State with 3,700 students. The College emphasizes balance between teaching and research, and offers B.S. degrees in the sciences including biology. Biology teaching and research laboratories are newly renovated, and expanded facilities will become available in 2006. Faculty and students conduct research in ecology, molecular biology, developmental biology, genetics, and microbiology. Pennsylvania Sea Grant is headquartered at Penn State Behrend. Erie, a metropolitan area of 280,000, is a service, tourism, medical, and industrial center on Lake Erie's Presque Isle Bay, two hours from Cleveland, Pittsburgh, and Buffalo. The region offers a variety of cultural, sports, and recreational resources with modest living costs and affordable housing. There are five colleges in the area. Send curriculum vitae, copies of graduate and undergraduate transcripts, teaching statement, research statement explaining the suitability of research program to an undergraduate institution, and names and e-mail addresses of three references that the search committee may contact independently. Send to: **Dr. Roger Knacke, Director, School of Science, Penn State Erie, Department BIOL-M, 5091 Station Road, Erie, PA 16563-0203.** Application review will begin on November 1, 2004, and continue until the position is filled. *Penn State is committed to Affirmative Action/Equal Opportunity and the diversity of its workforce.*

ASSISTANT PROFESSOR, BIOCHEMISTRY. The Department of Chemistry and Biochemistry at George Mason University invites applications for a full-time, tenure-track position in the general area of biochemistry for fall 2005. Please see **website: http://www.gmu.edu/departments/chemistry** for more information. The successful candidate will be expected to develop a vigorous research program with extramural funding and participate in undergraduate and graduate chemistry education. The biochemist will be part of a rapidly expanding interdisciplinary biosciences center on the Prince William Campus of George Mason University in Manassas, Virginia. Applicants should submit curriculum vitae, a brief (three-to-five page) statement of research interests, a teaching statement, and arrange for three letters of recommendation to be sent to: **Faculty Search Committee, Department of Chemistry and Biochemistry, MSN 3E2, George Mason University, 4400 University Drive, Fairfax, VA 22030.** Review of applications will begin on October 15, 2004, and continue until the position is filled. *George Mason is an Affirmative Action/Equal Opportunity Employer. Women and minority candidates are particularly encouraged to apply.*

FACULTY POSITION IN EXPERIMENTAL STROKE
Johns Hopkins University School of Medicine

Departments of Anesthesiology, Neurology, and Neurosurgery at Johns Hopkins University (JHU) seeking senior researcher in experimental stroke for position at **ASSOCIATE/FULL PROFESSOR** rank. Must have independent funding and experience with in vivo models of experimental stroke. Will collaborate with interdepartmental group of cerebrovascular and neuroscientists. Please send curriculum vitae, statement of research interests, and three letters of recommendation to: **Raymond C. Koehler, Ph.D., Department of Anesthesiology, Johns Hopkins University, 600 N. Wolfe Street, Blalock 1404, Baltimore, MD 21287; or e-mail: rkoehler@jhmi.edu.**

Australian Government

Australian Research Council

Federation Fellowships

The Australian Research Council's **Federation Fellowships** are innovative and highly prestigious awards designed to attract and retain outstanding researchers and build and strengthen world-class research capacity in Australia.

Up to 25 **Federation Fellowships** with a salary of around $240,000 per year for a standard tenure of five years are available for funding commencing in 2005.

Federation Fellowships particularly encourages applications from Australian and non-Australian researchers currently working overseas, especially from early- to mid-career researchers who will play a leadership role in building Australia's internationally-competitive research capacity.

The Fellowships are available for tenure at Australian higher education institutions and publicly-funded research organisations. Applications are due by 15 October 2004.

An Australian Government Backing Australia's Ability Initiative

For further information and documentation visit the Australian Research Council website at **www.arc.gov.au** or email **jorg.edsen@arc.gov.au**

hmaC020053

Hauptman-Woodward Medical Research Institute
Research Scientists
Protein Structure and Function

The Hauptman-Woodward Medical Research Institute is a private, not-for-profit organization studying the structures and functions of macromolecules of biomedical interest. The HWI is part of the Buffalo-Niagara Medical Campus, a consortium of research, clinical, and educational institutions founded to cultivate a world-class medical campus in downtown Buffalo. In the spring of 2005, HWI will move into a state-of-the-art new facility, greatly expanding and updating our laboratory space.

Over the next seven years, we will add 14 new research scientists to our staff. To complement and strengthen the structural expertise at HWI, we are recruiting in the areas of structural biology and functional biochemistry. We seek to recruit scientists who are studying macromolecular function through biochemical and biophysical techniques such as enzymology, proteomics, and protein engineering. Structurally minded researchers who are using functional analyses to characterize medically relevant proteins, enzymes that catalyze difficult reactions, or proteins of undefined function will fit well in the collaborative and productive environment at HWI. Individuals interested in developing the methodology of structural biology are also encouraged to apply. Scientists at the Hauptman-Woodward Institute serve as faculty within the Department of Structural Biology at the State University of New York at Buffalo. Graduate students at the University at Buffalo can enter the Structural Biology Department directly or through the Interdisciplinary Graduate Program in Biological Sciences.

We plan to hire immediately 2-3 Research Scientists (Asst., Assoc, or Full Professor equivalents) with interests in protein structure and function. For more information about current research programs and the new facility, visit our web site **http://www.hwi.buffalo.edu**. Interested applicants should submit a curriculum vitae, research plan, and arrange to have three letters of reference sent to: **George T. DeTitta, Ph.D., Hauptman-Woodward Medical Research Institute, 73 High St., Buffalo, NY 14203-1196; detitta@hwi.buffalo.edu**.

The Hauptman-Woodward Institute is an Equal Opportunity Employer.

Are you looking to work in a global growth company where you can make a real difference? With about 78,500 associates around the globe in our affiliates in over 140 countries, we share a vision of a better today and tomorrow for patients – a vision that drives our growth and success. Our greatest job satisfaction is knowing that we improve lives, we extend lives, and we save lives – and we do it with increasing precision and efficiency through breakthrough science and innovation.

Head Animal Facility

Novartis Institutes for BioMedical Research
Vienna, Austria

The Novartis Institute for BioMedical Research Vienna has an opening for a Veterinarian (Vet. Med.) to head our animal facility. Besides all operational aspects of running a large animal facility the interaction with the respective Austrian authorities is an important aspect of this position.

You need:

- A DMV degree with a strong background in Immunology
- A proven track record in all operational aspects of running a large animal facility, including interactions with the authorities
- Fluency in German and English (mandatory)
- Excellent organizational skills for heading a large group
- A strong and proven scientific track record for using various *in vivo* models (including a wide range of lab animals)
- A strong experience with complementary *ex vivo* analyses in the field of immunology, blood parameters (including biomarkers)

To find out more information and to apply, please visit www.novartis.at or send your CV to Novartis Forschungsinstitut GmbH, att. Margit Titz, Brunner Straße 59, 1235 Vienna, Austria, or via e-mail to margit.titz@pharma.novartis.com

Novartis is an equal opportunity employer.

NOVARTIS

www.novartis.com

FACULTY POSITIONS IN CATALYSIS/ BIOINORGANIC/NANOMATERIALS
Emory University (job posting #142294)

The Department of Chemistry at Emory University announces searches for two tenure-track positions in research areas broadly defined by catalysis/bioinorganic/nanomaterials. Preferably, one position will complement our recent growth at the interface of chemistry and biology, and candidates with research interests in catalysis or bioinorganic chemistry are strongly encouraged to apply. The second position would complement our growth in materials chemistry, and preferred candidates will have research interests in inorganic materials or nanoscience. One opening is at a **SENIOR** level and the other at the **ASSISTANT PROFESSOR** level (Ph.D. required). We seek candidates with interests in creative multidisciplinary research and a commitment to quality teaching at both the undergraduate and graduate levels. Core teaching responsibilities will be in the inorganic area with ample opportunity for multidisciplinary teaching as broadly defined above. For the senior-level appointment, applications are welcome from well-established, distinguished scholar-investigators and from individuals currently at the Assistant or Associate Professor levels with unusually strong records. Research laboratories and office space will be in the new Cherry Logan Emerson Hall (opened Winter 2001) or in the newly renovated Atwood Hall providing the successful candidate with ample opportunity to both complement the research interests within chemistry and establish ties with biological and materials research components across our campus as well as at nearby Georgia Tech. The Chemistry Department at Emory is a vibrant and growing program with more than 130 graduate students, 50 postdoctoral associates, and outstanding instrumentation and computational centers.

Candidates should submit a letter of intent, curriculum vitae and research plans, and arrange to have three letters of recommendation sent. Nominations for this position at the senior level are solicited. All materials and correspondence should be sent via e-mail (preferred) with attached Microsoft Word or Adobe Acrobat files to **e-mail: chemsearch@learnlink.emory.edu,** or alternatively by regular mail to: **Chair, Faculty Search Committee, Department of Chemistry, 1515 Dickey Drive, Emory University, Atlanta, GA 30322.** For more information about the Department, please visit the **website: http://www.emory.edu/CHEMISTRY.**

Application review will begin October 1, 2004, and will continue until the position is filled. *Emory University is an Affirmative Action/Equal Opportunity Employer and welcomes applications from individuals in underrepresented groups.*

FACULTY POSITION
Pharmacology and Toxicology
Dartmouth Medical School

The Department of Pharmacology and Toxicology seeks candidates for a tenure-track **ASSISTANT/ ASSOCIATE PROFESSOR FACULTY POSITION.** Candidates should have a Ph.D. and/or M.D. degree(s) and an outstanding academic record. The Department consists of faculty with broad expertise in cellular and molecular pharmacology and toxicology with focus in cancer, neuroscience, and cardiovascular disease (**website: http://www.dartmouth.edu/dms/pharmtox/**). Strong ties exist to the Norris Cotton Cancer Center, a National Cancer Institute (NIH)-designated comprehensive cancer center. Candidates should submit curriculum vitae, a statement of research interests and accomplishments, a record of grant support, and names of at least three references to the chair of the Search Committee: **Dr. Alan Eastman, c/o Ms. Ann Frost, Department of Pharmacology and Toxicology, Dartmouth Medical School, 7650 Remsen, Hanover, NH 03755-3835.** Review of applications will begin September 1, 2004. *Dartmouth, an Equal Opportunity/Affirmative Action Employer, strongly encourages applications from women and minority candidates.*

POSITIONS OPEN

PLANT BIOLOGY
University of Michigan

The Department of Molecular, Cellular, and Developmental Biology at the University of Michigan solicits applications for a faculty position in plant biology pending approval. We seek an individual who uses innovative approaches to study fundamental problems in plant biochemistry, cell biology, development, or physiology. We anticipate hiring at the **ASSISTANT PROFESSOR** level, but appointment at a more senior level is possible for applicants with suitable experience.

The Department of Molecular, Cellular, and Developmental Biology is a unit of the College of Literature, Science, and the Arts. The successful candidate will join a faculty that includes a vigorous group of plant biologists, and the number of faculty members in the Department is slated for substantial growth over the next few years.

Applicants should have a doctoral degree in biology or a related field and a record of publication in nationally eminent peer-reviewed journals. The successful candidate will be expected to demonstrate a commitment to outstanding instruction of both undergraduate and graduate students and to establishing a vigorous, extramurally funded research program.

To apply, candidates should send a cover letter, curriculum vitae, copies of reprints, brief summaries of recent research and future research plans, and a statement of potential teaching interests. Candidates for appointment as an Assistant Professor should also have at least three letters of reference sent immediately to the Department. All materials should be sent to: **Chair, Plant Biologist Search Committee, Department of Molecular, Cellular, and Developmental Biology, University of Michigan, 830 N. University Avenue, Ann Arbor, MI 48109-1048** or submitted via **e-mail: mcdb-search@umich.edu.** Applications and letters of reference should be received by October 1, 2004.

The University of Michigan is an Affirmative Action/ Equal Opportunity Employer. Women and members of groups who are currently underrepresented in the life sciences are encouraged to apply. The University is supportive of the needs of dual career couples.

FACULTY POSITION
Physiology and Biophysics
Case Western Reserve University

To support a significant expansion of the Department of Physiology and Biophysics at Case Western Reserve University, applications are being accepted for positions at the junior and/or more senior level. Candidates should have a Ph.D. and/or M.D. degree and a competitive research program focused on molecular, cellular, or integrated biology in one of the following research areas: (1) kidney pathophysiology, (2) heart failure biology, (3) keratinocyte biology, (4) lung pathophysiology.

The Department (**e-mail: physiology@cwru.edu**) offers a very interactive environment, a highly competitive compensation package, ample startup funds, and state-of-the-art research facilities. Submit complete curriculum vitae, statement of research interests, and the names and e-mail addresses of four references by **e-mail: dpbrecruit@case.edu.** *Case Western Reserve University is an Equal Opportunity/ Affirmative Action Employer.*

ASSISTANT/ASSOCIATE PROFESSOR

One long-term-track **FACULTY POSITION**. Begin December 2004, if possible. Ph.D. required; primary teaching responsibility microbiology along with freshman biology courses. Experience in small college preferred. Liberal arts environment. Responsibilities include academic advising, committee work, and expected to engage in biomedical research with undergraduates, to write grants, and to publish. Strong record of teaching excellence and scholarship desirable. Letter stating interests, complete resume, transcripts, and three letters of reference due prior to October 8, 2004, to: **Sr. John Karen Frei, Dean, School of Natural and Health Sciences, Barry University, Miami Shores, FL 33161.**

POSITIONS OPEN

ASSISTANT PROFESSOR OF BIOLOGY

Penn State Erie, The Behrend College, invites applications from invertebrate or cellular physiologists for a tenure-track position. Applicants must have a strong commitment to undergraduate teaching and research. Ph.D. is required; postdoctoral and teaching experience is a plus. Expectations: teach upper-division physiology courses with laboratories (two, in alternate years), a lecture course in biochemistry, share teaching responsibility for a core course in the biology major, establish a research program involving undergraduates, and seek external funding. Competitive startup funds are available.

Penn State Behrend is a four-year and graduate college of Penn State with 3,700 students. The College emphasizes balance between teaching and research and offers B.S. degrees in the sciences including biology. Biology teaching and research laboratories are newly renovated, and expanded facilities will become available in 2006. Faculty and students conduct research in ecology, molecular biology, developmental biology, genetics, and microbiology. Pennsylvania Sea Grant is headquartered at Penn State Behrend. Erie, a metropolitan area of 280,000, is a service, tourism, medical, and industrial center on Lake Erie's Presque Isle Bay, two hours from Cleveland, Pittsburgh, and Buffalo. The region offers a variety of cultural, sports, and recreational resources with modest living costs and affordable housing. There are five colleges in the area. Send curriculum vitae, copies of graduate and undergraduate transcripts, teaching statement, research statement explaining the suitability of research program to an undergraduate institution, and names and e-mail addresses of three references that the search committee may contact independently. Send to: **Dr. Roger Knacke, Director, School of Science, Penn State Erie, Department BIOL-M, 5091 Station Road, Erie, PA 16563-0203.** Application review will begin on November 1, 2004, and continue until the position is filled. *Penn State is committed to Affirmative Action/Equal Opportunity and the diversity of its workforce.*

FACULTY POSITION IN ORGANIC CHEMISTRY
Department of Chemistry
Boston College

Applications are invited for a tenure-track faculty position, effective September 2005, in organic chemistry. Applicants are expected to establish an internationally recognized and vigorous research program and be strongly committed to teaching at graduate and undergraduate levels. Applications at the **ASSISTANT PROFESSOR** level must include a detailed description of proposed research, curriculum vitae, and a summary of research accomplishments. In addition, applicants should arrange to have three letters of reference transmitted on their behalf. All materials should be sent to: **Chair, Organic Faculty Search Committee, Department of Chemistry, Boston College, Chestnut Hill, MA 02467-3860.** Completed applications must be received by October 15, 2004, to receive full consideration. **Website: http://chemserv.bc.edu. Fax: 617-552-2705.** *Boston College, a university of 14 schools and colleges, is an Equal Opportunity Employer and supports Affirmative Action.*

The University of Washington's Department of Bioengineering invites applications for tenure-track faculty positions. Applicants are particularly, but not exclusively, sought for the Department's research programs in Medical Imaging and Image-Guided Therapy and Distributed Diagnosis and Home Healthcare (D2H2), as detailed on the departmental **website: http://depts.washington.edu/bioe.** Applicants should submit curriculum vitae, a proposed research program, teaching statement, and contact information for five references to: **Professor Paolo Vicini, c/o Heather Tenore, Department of Bioengineering, Box 357962, University of Washington, Seattle, WA 98195,** or by **e-mail: hw@u.washington.edu** (please send attachments as PDF). *The University of Washington is building a culturally diverse faculty and strongly encourages applications from female and minority candidates. The University of Washington is an Equal Opportunity/Affirmative Action Employer.*

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THREE ASSISTANT PROFESSOR POSITIONS
University of Florida
Department of Neuroscience

Three new tenure-track appointments have been established at the level of Assistant Professor by the Department of Neuroscience and University of Florida College of Medicine for individuals with defined research interests in the translational neurobiology of stroke. We are seeking promising investigators for these positions who will be expected to contribute actively to the growth of an emerging University of Florida and Department of Veterans Affairs-based initiative focused on developing novel therapeutic strategies for promoting neuroplasticity after stroke. The successful candidates' research programs will thus establish collaborations with clinical investigators in neurorehabilitation, as well as with other basic neuroscientists with complementary interests and expertise at the Malcom Randall VA Medical Center, University of Florida Health Science Center, and McKnight Brain Institute. Substantial long-term VA funding will be available in addition to a generous startup package from the University of Florida. Persons interested in these positions should have appropriate expertise relevant to the neurobiology of stroke outcomes. We are particularly interested in identifying investigators who are performing applied stroke research that includes experience in the critical analysis of animal behavior. It is expected that the new appointees will establish an extramurally funded research program that will be directed at elucidating the underlying neurobiological mechanisms of stroke and subsequent neurorehabilitation which will help define candidate strategies for phase I clinical trials. Successful candidates will also participate in clinical and educational programs. Many resources are available to aid in this research, including numerous core facilities, nationally and internationally recognized programs in stem cell neurobiology, the translational neurobiology of spinal cord, and traumatic brain injury. These ongoing initiatives involve the study of neural precursor cell transplantation therapy in animals and humans; a longstanding program in the study of hemispatial neglect following cortical injury; a nationally recognized effort in gene therapy, a developing program in molecular imaging, and extensive multidisciplinary research in human neurorehabilitation.

Gainesville is a delightful place to live and work with excellent schools, recreational opportunities, health care, and abundant land and reasonable housing.

The start date for these positions is late 2004. Review of applications will begin September 1, 2004, and applications will be accepted until all the positions are filled. Candidates who are interested in these positions are encouraged to send a letter describing their major research interest, curriculum vitae, and three letters of recommendation to: **Ron Mandel, Ph.D., Department of Neuroscience, McKnight Brain Institute, P.O. Box 100244, Gainesville, FL 32610.** *Applicants must be U.S. citizens or permanent residents. The University of Florida, College of Medicine is an Equal Employment Opportunity/Affirmative Action Employer.*

SCIENTIST–IMMUNOLOGY

The Wisconsin National Primate Research Center (WNPRC) is recruiting a Scientist to lead a team investigating the immune responses to the AIDS virus in nonhuman primates. Responsibilities will include developing and implementing independent research investigating the SIV-specific T cell immune response. A Ph.D. in immunogenetics, immunology, or related field with postdoctoral training in T cell immunology is required. Interested individuals should send resume, cover letter, and three references to: **Susan Baculik, Wisconsin National Primate Research Center, 1220 Capitol Court, Madison, WI 53715-1299.** For more information, visit the University of Wisconsin **website: http://www.ohr.wisc.edu/apo/employment/index.htm.** *The University of Wisconsin is an Equal Opportunity Employer committed to excellence through diversity and encourages applications from women and underrepresented groups.*

POSITIONS OPEN

FRED HUTCHINSON CANCER RESEARCH CENTER
Advancing Knowledge, Saving Lives

PEDIATRIC ONCOLOGY FACULTY POSITION
Fred Hutchinson Cancer Research Center
University of Washington

The Clinical Research Division of the Fred Hutchinson Cancer Research Center (FHCRC) and the Department of Pediatrics, University of Washington are seeking a physician to be appointed as an **ASSISTANT, ASSOCIATE,** or **FULL MEMBER/ASSISTANT, ASSOCIATE,** or **FULL PROFESSOR** in the Physician/Scientist pathway. This person will be expected to have demonstrated productivity in the biology of childhood solid tumors and is expected to enhance our research activities in pediatric oncology at the FHCRC and Children's Hospital and Regional Medical Center. The successful candidate would have laboratory space within the Clinical Research Division of the FHCRC. Rank would be commensurate with experience.

Interested candidates should send curriculum vitae, a concise statement of research plans, and the names of four references along with a letter of application to: **Dan Meenach, Faculty Coordinator, Fred Hutchinson Cancer Research Center, Clinical Research Division, 1100 Fairview Avenue N., D5-310, Seattle, WA 98109.** The search will remain open until an appointment is made, but complete applications should be received by November 1, 2004, to ensure full consideration.

The Fred Hutchinson Cancer Research Center and the University of Washington are Affirmative Action/Equal Opportunity Employers. They are dedicated to the goal of building a culturally diverse and pluralistic faculty and staff committed to teaching and working in a multicultural environment and strongly encourage applications from women, minorities, individuals with disabilities, and covered veterans.

FACULTY POSITION IN MICROBIAL PATHOGENESIS

A tenure-track faculty position in microbiology is open at the **ASSISTANT** or **ASSOCIATE PROFESSOR** level in Richmond, Virginia. Applicants should have a Ph.D. or equivalent, a record of research accomplishments, and an interest in graduate and medical education. Expertise in molecular microbial pathogenesis (bacterial/viral/fungal) and/or host immune responses to microbial pathogens is preferred. This is an exceptional opportunity to join a strong research-oriented department in a very desirable geographic location. See **website: http://www.vcu.edu/micro/** for additional information. Please submit curriculum vitae with a statement of research interests and have three letters of reference sent to: **Dr. Phillip Hylemon, Chair of the Microbiology Search Committee, Department of Microbiology and Immunology, P.O. Box 980678, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, VA 23298-0678.** Items may also be sent to **e-mail: micacct@mail2.vcu.edu.** Applications will be reviewed upon receipt and considered until December 1, 2004, or until a suitable candidate is identified. *Virginia Commonwealth University is an Equal Opportunity/Affirmative Action Employer. Women, Minorities, and Persons with Disabilities are encouraged to apply.*

Two **POSTDOCTORAL RESEARCH POSITIONS** at the University of Miami School of Medicine are available to study innate immune responses to viral and malignant disease. The first position requires a Ph.D. with experience in immunology and/or vaccine development and evaluation. The second position would require a Ph.D with experience in *Drosophila* genetic systems. For consideration, please send curriculum vitae to: **Dr. Glen N. Barber** at **e-mail: gbarber@med.miami.edu.**

POSITIONS OPEN

ASSISTANT OR ASSOCIATE PROFESSOR TENURE TRACK
Cardiovascular Science–Pharmacology
Medical College of Georgia

We are seeking an individual with outstanding potential and accomplishments in cardiovascular research to complement and extend our current research strengths. We have established research programs in cardiac, endothelial, and vascular smooth muscle pharmacology, with specific interests in nitric oxide, oxidative stress, second messenger signal transduction mechanisms, hypertension, endothelial dysfunction, myocardial disease, diabetes, and cardiovascular ion channels. We encourage applicants with expertise in all areas of cardiovascular science, particularly in the factors that control cardiovascular dysfunction associated with diabetes and heart failure. Physician scientists are encouraged to apply. We offer a generous startup package and outstanding facilities are available for electron microscopy, cell imaging, microarray technology, genetically modified animals, primate research, and clinical collaborations. The successful applicant will participate in teaching programs for professional and graduate students. Please send curriculum vitae, summary of professional and research goals, and the names and addresses of three references to: **Richard E. White, Ph.D., Department of Pharmacology and Toxicology, Medical College of Georgia (MCG), Augusta, GA 30912-2300. E-mail: rwhite@mail.mcg.edu** and visit the Medical College of Georgia homepage (**website: http://www.mcg.edu**). Application review will begin October 2004. *MCG is an Equal Employment Opportunity/Affirmative Action Equal Access Employer.* PO# E000051148.

The Department of Biology at the University of North Florida (UNF) invites applications for two **TENURE-TRACK ASSISTANT PROFESSORS,** one in molecular cell biology and one in developmental biology, beginning August 2005. Candidates must have a Ph.D. in biology or related specialty, a commitment to undergraduate education, and potential to establish an independent, externally funded research program appropriate for undergraduate and graduate student participation. Teaching will include undergraduate and Master's degree level courses in area of specialty, and shared responsibility for introductory biology courses. The UNF campus is situated on a 1,300 acre wildlife sanctuary nine miles from the Atlantic Ocean. For more information, visit **website: http://www.unf.edu.**

A letter of application, curriculum vitae, concise statements of teaching experience and research interests, undergraduate and graduate transcripts, and three letters of reference should be sent to: **Search Committee (specify molecular/cell or developmental), Department of Biology, University of North Florida, 4567 St. Johns Bluff Road S., Jacksonville, FL 32224-2661,** by postmark deadline November 5, 2004. Applicants must apply online at **website: http://www.unfjobs.org** and must submit all required documents to be considered for this position. *UNF is an Equal Opportunity/Equal Access/Affirmative Action Institution.*

Carnegie Mellon University (CMU). The Department of Chemistry invites applications for a **TENURE-TRACK POSITION** at the junior level in the area of bioorganic chemistry and chemical biology. Candidates are expected to build a vigorous research program at the interface of chemistry and the biological sciences and exhibit a very strong commitment to teaching at both the undergraduate and graduate levels. Applications should contain (1) curriculum vitae, (2) a list of publications, (3) a brief description of research plans, and (4) three letters of recommendation sent to: **Professor Bruce Armitage, Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, PA 15213.** Review of applications will begin on October 15, 2004. *CMU is an Equal Opportunity/Affirmative Action Employer committed to building a diverse faculty; women and minorities are strongly encouraged to apply for this position.*

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HACKENSACK UNIVERSITY MEDICAL CENTER

DIRECTOR for ONCOLOGY RESEARCH

HACKENSACK UNIVERSITY MEDICAL CENTER, located in Bergen County, approximately 15 minutes from New York City, is one of the foremost healthcare providers in the country and the largest provider of inpatient and outpatient services in the state of New Jersey.

Our renowned Cancer Center is among the top 8 providers of clinical and research cancer services in the nation by patient volume, and is in its 20th year of funding as an NCI-designated CCOP. Currently, an excellent opportunity is available for a Director for Oncology Research.

In this position, you will be responsible for directing our on-going research efforts in the area of oncology treatment, and for the administrative and clinical operation of all research conducted at The Cancer Center.

The successful candidate we seek will have a relevant Master's degree and a minimum of 3 years in bioscience research, preferably in the field of oncology. A PhD degree is preferred; and a minimum of 2 years' experience in a supervisory capacity is desired.

We offer a competitive salary and excellent benefits in an environment that is conducive to growth. Please apply online at **www.humed.com "Careers"** or send/e-mail letter of interest and resume to **Lenore Mooney, Professional Recruiter, Hackensack University Medical Center, 60 Second Street, Hackensack, NJ 07601**. We are an equal opportunity employer offering a smoke-free environment.

We are an equal opportunity employer offering a smoke-free environment.

A SUBSIDIARY OF HILLCREST HEALTH SERVICE SYSTEM; A teaching and research hospital affiliated with The University of Medicine and Dentistry of New Jersey - New Jersey Medical School; A New Jersey State-Designated Children's Hospital.

National Center Director
National Center for Environmental Research
Office of Research and Development

EPA's Office of Research and Development is seeking a highly qualified science manager to direct the National Center for Environmental Research (NCER).

Applicants must have a Bachelors degree, or higher, in a discipline related to environmental science or engineering with demonstrated ability to understand a multidisciplinary program with national environmental policy implications. In addition to possessing core executive qualifications of the Senior Executive Service, the individual must demonstrate highly creative problem solving skills and exceptional ability to communicate science issues, results, and impacts to a broad range of audiences and stakeholders including EPA program managers, other federal agencies, Congress, and other science organizations.

For an overview of NCER's activities, please go to www.epa.gov/ncer.

This is a Senior Executive Service position. The position opens on July 19, 2004 and closes September 30, 2004. The salary range is $104,927 to $145,600 depending on qualifications.

Applicants must address the executive and technical qualifications described in the vacancy announcement for this position. Call or write to USEPA/OARM/OHR/SES Human Resources Staff (3650A), 1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460. You may download a full announcement at www.usajobs.opm.gov. The vacancy number is EPA-04-SES-ORD-6322.

U.S. Citizenship Required.
Applications must be received by the closing date of September 30, 2004.
EPA is an Equal Opportunity Employer.

PROGRAM MANAGER III

Responsibilities are to provide technical oversight in the execution of multiple multi-center research programs to include the execution of protocols; the development of appropriate operating procedures and tools for use in the research; and the provision of writing and editorial skills in connection with all phases of the preparation and issuance of technical reports, articles, books and journals, scripts, and software documentation. Participates in the design, development, and implementation of standard operating procedures as well as investigational protocols. Reviews and modifies the procedures as needed to meet the needs of the project. Participates in the design and implementation of data collection tools. Ensures that proper procedures are followed for all patient contacts, protocols are strictly adhered to, and data is accurately collected and recorded. Oversees multiple research staff members in regards to adherences to legal, professional, and ethical codes with respect to confidentiality and privacy. Edits, re-writes, and proofreads specialized medical, scientific and technical reports, articles, books, and other materials for publication. Revises software documentation, scripts, and reports based on editorial, technical, oversight, and end-user comments without altering the technical content to be presented. Assists in the oversight of grants, budgets, contracts, and employment of research staff.

Minimum Education/Training Requirements: Master's degree in molecular biology, genetics, or biochemistry. Degree in journalism or English; as well as regulatory experience desirable.

Minimum Experience: Four to six years experience working with research protocols. Prior experience in writing and editing.

Please apply online at **website: http://www.hjf.org/careers.** Attn: Job Req. 200304.

The Henry M. Jackson Foundation for the Advancement of Military Medicine is a nonprofit medical research organization providing support services to the military medical community. We offer a competitive salary and generous benefits package. Affirmative Action/Equal Employment Opportunity.

FACULTY POSITIONS
Invertebrate Biology, Cell Biology, Plant Ecology, and Pathogenic Microbiology

The Department of Biological Sciences at Clemson University invites applications for four tenure-track positions at the **ASSISTANT PROFESSOR** level to support the continuing development of emphasis areas in biomedicine, biotechnology, and sustainable environment. Exceptional candidates of higher rank may be considered. We are seeking broadly educated biologists who can interact with other faculty having diverse interests ranging from cell and molecular biology through organismal biology to ecology and evolution. Research may be in any area(s) of the specialty. Successful candidates will be expected to establish research programs of national distinction and be inspiring teachers. Postdoctoral experience is required. Primary teaching responsibilities will be an undergraduate course for majors and graduate course(s) in one's specialty. Applications should include a resume, up to three reprints, a statement of current and planned research, a statement of teaching interests and philosophy, and three letters of recommendation sent by the applicant's references. Applications and letters of recommendation should be sent to: **Ms. Vicky Freeman, Search Committee, Department of Biological Sciences, Clemson University, Clemson, SC 29634-0314.** (Letters and envelopes should clearly indicate the position sought, e.g., "Cell Biology.") Electronic applications and letters of recommendation may be sent to Ms. Freeman at **e-mail: vfrmn@clemson.edu.** (Include the name of the position followed by "Search Committee" on the subject line.) Completed applications should arrive by October 15, 2004. Information about these positions, departmental resources and the research interests of the faculty may be obtained at our **website: http://www.clemson.edu/biosci.**

Clemson University is an Equal Opportunity/Affirmative Action Employer. Women and minority candidates are encouraged to apply.

NEUROSCIENCE FACULTY POSITION
The University of North Carolina at Chapel Hill

The Department of Cell and Molecular Physiology in the School of Medicine invites applications for a tenure-track faculty position (rank dependent on qualifications). Applicants must be at least two years **POSTDOCTORAL**. We seek candidates using novel approaches to study the physiology or pathophysiology of the nervous system. Preference will be given to individuals with established record of exciting, contemporary work on integrative neural function. An attractive startup package and new laboratory space are available. The Department's faculty are expected to contribute to teaching of graduate and medical students.

Please submit the names of four potential references, curriculum vitae, statement of the proposed research program, and career goals by e-mail to:

Neuroscience Search Chair
Edward R. Perl
Department of Cell and Molecular Physiology
5109 Neuroscience Research Building CB #7545
School of Medicine
The University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7545
E-mail: neurosearch@med.unc.edu

Closing date for first consideration: October 11, 2004. *UNC is an Equal Opportunity Employer.*

FACULTY POSITION
Theoretical and Computational Biophysics
University of Illinois, Urbana-Champaign

The Department of Physics invites applications for a full-time tenure-track faculty position at the **ASSISTANT PROFESSOR** level in the area of theoretical and computational biophysics, beginning as early as August 16, 2005. An appointment at a higher level will be considered for an exceptionally well-qualified candidate. A Ph.D., or equivalent, is required, along with the ability to teach effectively at both undergraduate and graduate levels and to conduct a vigorous and significant research program. For full consideration, completed applications should be received before October 15, 2004. Salary will be competitive and commensurate with qualifications. Applicants should submit curriculum vitae, a publications list, a summary of their research plans and accomplishments, and the names and addresses of three references. Submission via the web is preferred (**website: http://fms.physics.uiuc.edu/apply/faculty/apply.htm**). Applications may also be submitted by post to: **Faculty Search Coordinator, Department of Physics, University of Illinois at Urbana-Champaign, 1110 W. Green Street, Urbana, IL 61801-3080, U.S.A.** *The University of Illinois is an Affirmative Action/Equal Opportunity Employer.*

Behavioral Neuroscience: The Department of Psychology at Yale University anticipates a position (level open) in behavioral neuroscience or cognitive neuroscience. We are especially interested in applications from candidates with research interests that complement the Department's current strengths in learning and memory, but outstanding candidates in any area will be considered. It is expected that candidates will have, or show promise of, an exceptional program of research. In addition, successful candidates should be able to demonstrate excellence in teaching at both the undergraduate and graduate levels. All applicants should send a letter of application, curriculum vitae, and one copy of selected publications. Applicants for a nontenured position should arrange for three letters of recommendation to be sent. Applicants for a tenured position should send the names and addresses of at least three referees. Materials should be sent either to: **Chair, Junior Behavioral Neuroscience Search Committee,** or the **Chair, Senior Behavioral Neuroscience Search Committee,** at the **Department of Psychology, Yale University, 2 Hillhouse Avenue, P.O. Box 208205, New Haven, CT 06520-8205.** Deadline for completed applications is November 1, 2004. *Yale University is an Equal Opportunity/Affirmative Action Employer and applications from women and minority group members are especially encouraged.*

IMMUNOLOGIST
Department of Health and Human Services
National Institutes of Health
National Cancer Institute

The National Cancer Institute (NCI) at Frederick, Maryland is recruiting for a Staff Scientist in the Laboratory of Experimental Immunology. A team-oriented individual to provide leadership to postdoctoral fellows and technicians performing basic and translational studies in immune response regulation and cancer therapy is sought. Applicants must possess a Ph.D. or M.D. degree, demonstrate research accomplishments in cellular and molecular immunology, and have excellent organizational, speaking, and writing skills. Candidates should possess a record of publication and accomplishment in the areas of T cell, dendritic cell and/or natural killer (NK)/NKT cell biology, and be well-versed in cellular and molecular assays of leukocyte functions, flow cytometry, and molecular techniques related to immune regulation. Salary is commensurate with experience and benefits are available. To apply, send curriculum vitae, bibliography, statement of research goals, and contact information for five references to: **Ms. Lori Holliday, National Cancer Institute at Frederick, Building 578, P.O. Box B, Frederick, MD 21702,** by close of business, October 1, 2004. *DHHS and NIH are Equal Opportunity Employers.*

MOLECULAR ECOLOGIST OR EVOLUTIONARY BIOLOGIST
University of Nebraska-Lincoln (UNL)

The School of Biological Sciences invites applications for a tenure-track faculty position at the **ASSISTANT PROFESSOR** level with expertise in using molecular techniques to investigate evolutionary and/or ecological questions with an emphasis in organismal biology. Candidates will be expected to develop a rigorous research program and assume teaching responsibilities in undergraduate courses in the areas of biological diversity and/or ecology and evolution, and at the graduate level in their area of expertise. A Ph.D. in the life sciences is required and postdoctoral experience is preferred. To apply, send curriculum vitae and copies of representative publications along with statement of research interests and teaching interests and philosophy. Also arrange for three letters of reference to be sent by September 17, 2004, to: **Jack Morris, School of Biological Sciences, University of Nebraska-Lincoln, 348 Manter Hall, Lincoln, NE 68588-0118.** The position will remain open until a suitable candidate is selected. *UNL is committed to a pluralistic campus community through Affirmative Action and Equal Opportunity, and is responsive to the needs of dual career couples. We assure responsible accommodation under the Americans with Disabilities Act.* For further information, contact **Jack Morris** at **telephone: 402-472-6676** for assistance.

FACULTY POSITION IN ECOLOGY AND EVOLUTIONARY BIOLOGY

The University of Oregon Center for Ecology and Evolutionary Biology (CEEB) and The Department of Biology seek applications for a position in ecology. Rank is open with preference given to **ASSISTANT** or **ASSOCIATE** level. We are particularly interested in candidates conducting hypothesis-driven research at any scale, but especially at the community level. We will consider exceptional ecologists in all areas, including, but not limited to, microbial ecology and biogeochemistry, environmental genomics, and disease ecology. The successful candidate will have an outstanding research program and a commitment to excellence in teaching. Ph.D. required. Applicants should submit curriculum vitae, statements of research interests and teaching philosophy, and three letters of recommendation to: **Ecology/Evolution Search, Department of Biology, University of Oregon, Eugene, OR 97403-1210. Website: http://evolution.uoregon.edu/.** To ensure full consideration, applications must be received by October 15, 2004. *The University of Oregon is an Equal Opportunity/Affirmative Action Institution committed to cultural diversity and compliance with the Americans with Disabilities Act. Women and minorities encouraged to apply.*

POSITIONS OPEN

CENTRAL NERVOUS SYSTEM ELECTROPHYSIOLOGISTS: NIH-funded **POSTDOCTORAL POSITIONS** available to study the integration of peripheral baroreceptor and chemoreceptor afferent inputs. We are currently investigating the plasticity of these integrative processes in hypertensive, chronic, and intermittent hypoxic models. Applicants should have expertise with in vivo and/or in vitro electrophysiological approaches. Interested applicants should send curriculum vitae and names of three references to the e-mail address below. *All postdoctoral appointments are designated as security sensitive positions.* Contact: **Steve Mifflin, Ph.D., Department of Pharmacology, MC 7764, University of Texas Health Science Center-San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900. E-mail: mifflin@uthscsa.edu.** *The UTHSCSA is an Equal Employment Opportunity/Affirmative Action Employer.*

POSTDOCTORAL RESEARCH position available immediately for a motivated individual interested in developing expertise in molecular signaling mechanisms in vascular cell types. Successful candidates will become members of the newly developed, multidisciplinary, and highly dynamic Vascular Biology Research Group at Temple University School of Medicine. Candidate must have a Ph.D. in a related discipline. Those possessing a background in vascular cell culture, cell and molecular biological techniques, signaling, and animal models are encouraged to apply to:

Victor Rizzo, Ph.D.
Associate Professor
Temple University School of Medicine
3400 North Broad Street
Philadelphia, PA 19140

Temple University is an Affirmative Action/ Equal Opportunity Employer and strongly encourages applications from women and minorities.

A **RESEARCH ASSOCIATE POSITION** is available for a recent Ph.D. in molecular biology and/or biochemistry to study DNA replication on the genomic scale. Experience with DNA arrays, RNA handling, or databases is a definite plus. Interested applicants please send curriculum vitae and names of references to: **Dr. Zhifeng Shao (e-mail: zs9q@virginia.edu), Department Molecular Physiology and Biological Physics, University of Virginia Health System, Box 800736, Charlottesville, VA 22908.** *University of Virginia is an Equal Opportunity/Affirmative Action Employer.*

POSTDOCTORAL POSITION to study cell cycle regulation in budding yeast, with emphasis on mitotic exit regulation and DNA damage response. Candidates should have a Ph.D. in molecular and cell biology and/or molecular genetics. Applicants should send resumes to: **Yanchang Wang, Ph.D., Florida State University, College of Medicine, 1269 West Call Street, Tallahassee, FL 32306-4300; Telephone: 850-644-0402; e-mail: yanchang.wang@med.fsu.edu.** *Florida State University is an Equal Opportunity/Affirmative Action Employer.*

DIRECTOR OF ANIMAL WELFARE. Ph.D. in animal science, animal behavior, and welfare or related field plus three months related experience. Must demonstrate in-depth knowledge of the science of swine behavior and welfare and oral and written communication skills. Experience with multidisciplinary and international research teams. Send resume and writing sample to: **Jill Criss, 1776 N.W. 114th Street, Clive, IA 50325.**

POSTDOCTORAL RESEARCH FELLOW sought to study the genetic basis of microcephaly. Requirements include M.D. with significant experience in pediatric neurology including ability to perform clinical analysis of research subjects, gene mapping, and cloning. Send resumes to: **Clifford B. Saper, M.D., Ph.D., Beth Israel Deaconess Hospital, 330 Brookline Avenue, Boston, MA 02215.**

POSITIONS OPEN

POSTDOCTORAL AND CLINICAL FELLOWSHIPS
at the
National Institutes of Health
U.S. Department of Health
and Human Services
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NIH is dedicated to building a diverse community in its training and employment programs.

RESEARCH POSITION (full-time Postdoctoral based on experience and qualifications), is available in the Department of Neurological Surgery, University of Wisconsin-Madison. The preferred candidate should have a Master's/Ph.D. in chemistry or biochemistry with experience in lipid biochemistry. The NIH-funded projects will study phospholipases response to inflammatory factors (TNF-a and IL-1B) and phospholipids homeostasis in stroke (see: **Adibhatla** et al., *J. Neurosci.* **76:**390–396, 2004). Experience with small animal surgeries, techniques of molecular biology, and immunohistochemistry are desirable. Send curriculum vitae and names of three references to:

Christy Seaholm
Department of Neurological Surgery
K4/836 Clinical Science Center
600 Highland Avenue
Madison, WI 53792
Telephone: 608-263-0170
Fax: 608-263-1728
E-mail: seaholm@neurosurg.wisc.edu

POSTDOCTORAL ELECTROPHYSIOLOGIST
University of Otago, New Zealand

Applications are invited for an electrophysiologist Postdoctoral Fellow position familiar with brain slice patch-clamp methodologies for a three-year position. Studies will involve the investigation of amino acid neurotransmission in the GnRH neuronal phenotype using a variety of transgenic mouse models. For further information, please contact: **Professor Allan Herbison** via **e-mail: allan.herbison@otago.ac.nz** or visit our **website: http://herbisonlab.otago.ac.nz.**

The Department of Chemistry of The University of Chicago invites applications from qualified individuals for positions of **POSTDOCTORAL RESEARCH ASSOCIATE** in Chemistry. These searches are in the areas broadly defined as inorganic, organic, and physical chemistry. For details about specific job opportunities and how to apply, visit **website: http://jobopportunities.uchicago.edu.** Qualified applicants will have a Ph.D. degree or will have completed the Ph.D. requirements in the related areas prior to hire. *The University of Chicago is an Equal Opportunity/Affirmative Action Employer.*

POSTDOCTORAL POSITION available immediately to study regulation of the endothelial nitric oxide synthase using cell culture, molecular biology, and protein chemistry techniques. Background of applicant less important than the desire and aptitude to learn. Contact: **Richard C. Venema, Ph.D., Associate Professor, Vascular Biology Center, Medical College of Georgia, Augusta, GA 30912.** No e-mail applications accepted.

POSTDOCTORAL POSITIONS

Postdoctoral positions are available to study the mechanisms of apoptosis in cancer cells. Strong background in cell and molecular is required. Please send curriculum vitae and three letters of recommendation to: **Dr. Rakesh K. Srivastava, Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD 21201, U.S.A. E-mail: rsrivast@rx.umaryland.edu.**

POSITIONS OPEN

POSTDOCTORAL POSITION available immediately in Section on Epithelial and Retinal Physiology and Disease, within the Division of Intramural Research, National Eye Institute (NEI), National Institutes of Health (NIH), Department of Health and Human Services (DHHS) located in Bethesda, Maryland, to study the plasma membrane, intracellular, and molecular mechanisms that regulate water movement across epithelia. A major project in the laboratory involves the retinal pigment epithelium which has multiple barrier and transport functions that serve to maintain the health and integrity of the retina and choroid (**Maminishkis** et al., *Investigative Ophthalmol. and Vis. Res.* **43:**3555, 2002). We are also interested in understanding the mechanisms that regulate water transport across airway and mammary epithelia in health and disease (**Blaug** et al., *Am. J. Physiol.* (cell): 2003). Applicants must have a strong background in physiology, biophysics, or bioengineering; experience in imaging, animal models, histology, or cell culture is also desirable. Applicants should have less than five years of postdoctoral experience. Please send curriculum vitae, description of research interests, and contact information for three references to: **Sheldon Miller, Section on Epithelial and Retinal Physiology and Disease/National Eye Institute/National Institutes of Health, 10 Center Drive, 10/10B04, Bethesda, MD 20892-1857. E-mail: serpd@nei.nih.gov.** *DHHS and NIH are Equal Opportunity Employers.*

POSTDOCTORAL POSITIONS IN BREAST CANCER BIOLOGY
Karmanos Cancer Institute of Wayne State University

Three Postdoctoral Fellowships are currently available in the laboratory of **Dr. Stephen Ethier** at the Karmanos Cancer Institute. Work in the Ethier laboratory is focused on discovering and validating novel human breast cancer oncogenes, understanding the altered signaling pathways that drive expression of transformed phenotypes in human breast cancer cells, performing translational studies to understand the molecular basis for the response of breast cancer cells to targeted inhibitors, and developing new models of human breast cancer development. New breast cancer models under development will be studied using novel bioinformatic/computational approaches. Applicants must have a Ph.D. with a background in cell biology, molecular biology, cancer biology, bioinformatics, or related fields. Interested applicants should send their curriculum vitae, a statement of research interests, and the names of three references to: **Stephen P. Ethier, Ph.D. Associate Center Director for Basic Science/Deputy Director, Karmanos Cancer Institute, 4100 John R. Street, Detroit, MI 49201.** *Equal Opportunity Employer.*

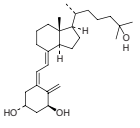
POSTDOCTORAL FELLOWSHIP

A Postdoctoral Fellowship opportunity is available in the laboratory of **Dr. Brian Haab** (**website: http://www.vai.org/vari/labs/haab.asp**) to apply novel protein measurement tools for the study of serum protein alterations in cancer patients. A Ph.D. in a life sciences or chemistry discipline is required. Qualified candidates should send a statement of research interests, curriculum vitae, and the names and addresses of three references via **e-mail: variemployment@vai.org** or to: **Van Andel Research Institute, Human Resources Department, Personnel Req. 432, 333 Bostwick, Grand Rapids, MI 49503.** *Equal Opportunity Employer.*

POSTDOCTORAL POSITIONS are available to study cytokine signal transduction, transcription factors, hypoxia, and heart development (see: *J. Biol. Chem.* **277:**8091–8, 2002; *Proc. Natl. Acad. Sci.* **99:** 10488–93, 2002; *J. Biol. Chem.* **278:**11197–204, 2003; *J. Biol. Chem.* **278:**22838–45, 2003; *J. Biol. Chem.* PMID: 15280358). Candidates with experience in molecular biology and/or knockout/transgenic animals should send their curriculum vitae to: **Dr. Yu-Chung Yang, Department of Pharmacology, Case Western Reserve University School of Medicine** to **e-mail: yxy36@cwru.edu.**

INTERNATIONAL CAREERS

MEETINGS



Cancer Chemoprevention & Cancer Treatment: Is there a role for vitamin D, 1α,25(OH)$_2$-vitamin D$_3$, or new analogs (deltanoids)?

Wednesday, November 17 – Friday, November 19, 2004

Natcher Conference Center, NIH Campus Bethesda, Maryland USA

Co-sponsored by the National Cancer Institute, NIH and the Vitamin D Workshop, Inc.

Abstract Deadline Date: Monday, September 27, 2004
(The abstract form is available at http://vitamind.ucr.edu)

Come join us for the **Cancer Chemoprevention & Cancer Treatment: Is there a role for vitamin D, 1α,25(OH)$_2$-vitamin D$_3$, or new analogs (deltanoids)?** meeting, which will be held Wednesday, November 17 – Friday, November 19, 2004 at the Natcher Conference Center on the NIH Campus in Bethesda, Maryland.

This 2.5 day meeting will cover all aspects of vitamin D, 1α,25(OH)$_2$D$_3$ and related analogs and any aspect of cancer. The meeting objective is to provide an up-to-date summary of the current status of vitamin D and cancer research and to identify the next challenges and goals in this field. The Scientific Program consists of 15 speaking sessions, including 31 Invited Speaker presentations and 4 poster sessions. Free communication posters are welcome. Six Young Investigator Travel Awards (up to $700) will be awarded based on poster evaluations.

Topics covered in this meeting include:

- Molecular targets of vitamin D and 1α,25(OH)$_2$D$_3$ action
- Gene regulation and 1α,25(OH)$_2$D$_3$
- Vitamin D endocrine system – target organs
- Cancer and vitamin D
- Chemistry of vitamin D analogs
- Malignant cells and vitamin D
- Cancer related clinical studies and 1α,25(OH)$_2$D$_3$ or analogs

There is no registration fee for this meeting, but all delegates who wish to attend must complete an Official Registration Form (which can be found on the Vitamin D Workshop website **http://vitamind.ucr.edu**). Contact Information: **Vitamin D Workshop, Inc., Department of Biochemistry, University of California, (951) 827-4777, vitaminD@ucr.edu, http://vitamind.ucr.edu**.

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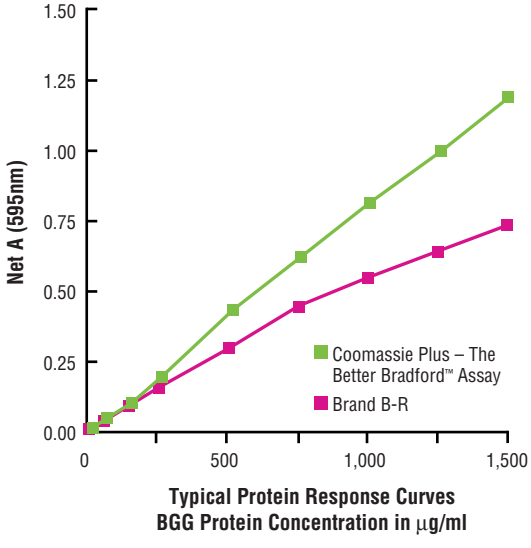

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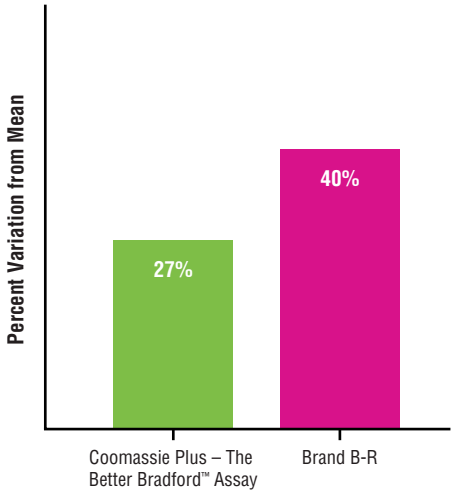

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